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PERIODIC ACCREDITING OF HOUSEHOLDS

AN ECONOMICAL AUXILIARY METHOD FOR CONTROLLING HUMAN TUBERCULOSIS, SUITABLE FOR USE IN PRIVATE PRACTICE

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About twenty years ago, American veterinarians adopted the policy of using the tuberculin test as a means for detecting previously unrecognized potential and active disseminators of bovine tubercle bacilli and of slaughtering all contaminated cattle to protect the uninfected members of herds. In response to repeated general applications of these rigorous prophylactic measures, the former widespread menace of bovine tuberculosis has practically disappeared from the United States. This outstanding demonstration of the control of communicable disease suggests the possibility of effectively and promptly controlling the human source of contagion by intensively applying comparable prophylactic measures suitable for preventing infection in man by contact. The magnitude of this problem is such that its ultimate solution will doubtless require the concerted efforts of the large number of physicians engaged in private practice.

An ideal and complete method for attaining this objective probably should include: (1) the routine application of the Mantoux test to the present and future members of the entire population; (2) periodic retesting of all persons found uninfected on previous surveys; (3) frequent roentgenologic, clinical and laboratory examinations of each infected patient discovered during repeated epidemiologic surveys, and (4) prompt segregation of all patients with tuberculosis until their condition is no longer infectious. This program provides a practical and dependable method for identifying human disseminators of tubercle bacilli with reasonable promptness and supplies an effective method for keeping them from infecting their associates. It is based, therefore, on two fundamental principles which are identical with those underlying the plan by which bovine tuberculosis has practically been eradicated. A systematic general use of the idealistic but expensive program out-

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lined here as suitable for effectively screening the population could probably be expected to control the human source of contagion in much the same manner that a general application of an essentially identical program solved the comparable problem of controlling the bovine source of infection.

The appeal of this utopian possibility, combined with a desire to guarantee, if possible, that children receiving private professional care were not living in intimate contact with persons having open tuberculosis, resulted in the modest attempt here reported to test the practicability and value of surveying household units. The original intent of this venture was to apply Mantoux tests to the entire personnel of separate homes at regular intervals and to obtain annual clinical and roentgen studies of each infected patient discovered in this manner. The inability, however, of many parents to finance indicated roentgenologic examinations, combined with the frequent failure of tuberculin-sensitive persons whose initial studies revealed no obviously communicable form of tuberculosis to appreciate the desirability of submitting regularly to relatively expensive complete reexaminations, greatly limited the use of this preferred plan for detecting cases of open tuberculosis. Consequently, the need for developing an inexpensive method for surveying families with limited resources seemed to be obvious.

The economical expedient that was devised to facilitate the promotion in private practice of an unsubsidized tuberculosis survey included the routine use of the relatively inexpensive Mantoux test and utilized the results of tests applied to children for determining whether the economy of omitting roentgenologic and clinical examination of their adult associates was permissible. According to this plan, the satisfactorily demonstrated failure of tuberculin-sensitive parents to infect their own children was accepted as dependable evidence that the former were not serving as effective sources of contagion and that additional and relatively expensive examinations of the specifically allergic adults could be deferred with reasonable safety. Household units of this character, as well as those which contained no infected member, were tentatively rated, solely on the basis of the results of the tuberculin test survey, as safe, contagion-free units. Retention of this rating was deemed contingent, however, on periodic demonstration that the number of infected persons in the home was not increasing. The different types of households tentatively accredited in this manner as safe units for children to live in are portrayed graphically in table 1. Families composed of 5 members were used in the table merely for illustrative purposes.

The compromise method for identifying homes which harbor disseminators of tubercle bacilli is open to the objection that it tends to defer the detection of cases of open tuberculosis until the infection of a previously uncontaminated associate has been accomplished. It is to be employed, therefore, mainly in fields where a lack of funds leaves

no alternative. When used under these circumstances, the inexpensive plan for surveying component units of the population serves two important functions. It leads to the discovery of patients with open tuberculosis whose identification might otherwise be delayed, and it provides a means by which a large number of physicians engaged in private practice can participate in the tremendous task of controlling the human source of infection. The economical alternative for the preferred method of more thoroughly canvassing households seems to constitute a valuable auxiliary, or complementary means, for augmenting the present antituberculosis campaigns, and for this, as well as for other reasons, its liberal application in neglected fields probably can be recommended. Limited financial resources generally necessitated its use in the investigation of the homes included in this study. Since the follow-up phase of this investigation is in its infancy, only the results of the initial survey are reported in this paper.

TABLE 1.—*Schematic Representation of the Application of the Economical Method for Accrediting Household Units*

Tuberculin Reaction					
Parents		Children			
Father	Mother	1	2	3	
Types of Households Accredited Solely on Results of Mantoux Tests					
—	—	—	—	—	No infected person in the home
+	—	—	—	—	Infected adult had not contaminated immediate associates
—	+	—	—	—	
+	+	—	—	—	Infected parents had not contaminated their children
Households Whose Rating Required Additional Study					
—	—	+*	—	—	Special examination of infected child was desirable
+	—	+*	—	—	Special examination of infected parents was imperative and of infected children was desirable
—	+	+*	—	—	
+	+	+*	—	—	

* One or more children per household might have been tuberculin-sensitive.

During a three year period 0.1 mg. of old tuberculin was administered intradermally to each of 1,593, or 69.1 per cent, of the 2,305 senior and junior members of 642 separate households (table 2).[1] The preliminary survey included the entire personnel of 213, or 33.2 per cent, of the homes represented in this study (table 3). For various reasons, frequent among which was the failure of the father to receive a tuberculin test, the remaining 429 groups were only partially investigated. Consequently, 307 homes are represented in the survey by 1 parent and 1 or more children, and 122 units are represented solely by children. The Mantoux test was applied to 57.3 per cent of the parents and to

1. Mantoux tests were also applied to 33 adult relatives and to 11 maids. Twenty-four of the former and 1 of the latter were found to be sensitive to tuberculin, but in none of these cases was a communicable form of tuberculosis found. The records of these 49 adults somewhat temporarily present in the homes surveyed are not included in the tables.

83.9 per cent of the children in the homes that were canvassed (table 2). Although the survey was by no means a complete one, the tested sample (69.1 per cent of the total personnel of these households) probably was

TABLE 2.—*Orienting Tabulation of the Data Obtained in the Preliminary Survey of Household Units*

Number of Household Units Represented in the Survey	Total Personnel of These Units	Number and Percentage of Total Personnel Tested	Parents: Average Age, Yr.	Parents: Number and Percentage Tested	Parents: Percentage Found Infected	Parents: Average Annual Infection Attack Rate per 100 Cases	Children: Average Age, Yr.	Children: Number and Percentage Tested	Children: Percentage Found Infected	Children: Average Annual Infection Attack Rate per 100 Cases
642	2,305*	1,593 (69.1)	35.9	733† (57.3)	57.3	1.6	6.3	860‡ (83.9)	5.2	0.8

* See footnote 1.
† Total number of living parents, 1,280; 4 deceased.
‡ Total number of living children, 1,025; number deceased not known.

TABLE 3.—*Distribution of Infected Persons in Various Groups of Households Surveyed with Different Degrees of Thoroughness*

Group	Parents: No. Tested	Parents: Percentage Infected	Parents: Average Age, Yr.	Children: Average Age, Yr.	Children: Total Number	Children: Number Uninfected	Children: Number Infected	Children: Percentage Infected	Chances per 1,000 That Difference Between Groups 1 and 3 Was Due to Accident (Chi Square)	Households: Number in Each Group	Households: Households in Which Infected Children Were Present	Chances per 1,000 That Difference Between Groups 1 and 3 Was Due to Accident (Chi Square)
Complete Household Units Tested												
1	92	0	34.2	5.4	77	73	4*	5.2	140†	46	4*	342§
2	168	50	36.6	5.7	130	124	6	4.6		84	6	
3	166	100	37.1	6.3	133	118	15	11.3		83	12	
Total and av.	426	58.7	36.3	5.8	340	315	25	7.4		213	22	
										8.7		
										7.1		
										14.5		
										10.3		
One Parent and Majority of Children in the Home Tested												
4	137	0	34.0	6.5	167	166	1	0.6		137		
5	170	100	36.9	6.7	207	198	9	4.3		170		
Total and av.	307	55.4	35.6	6.6	374	364	10	2.7		307		
Parents Not Tested; Majority of Children in the Home Tested												
6	...	.....	....	6.3	146	136	10‡	6.9		122		
Grand total	733	57.3	35.9	6.3	860	815	45	5.2		642		

* No adults except the parents were living in these homes.
† Chi square = ± 1.48 = 140 chances per 1,000.
‡ Roentgen examinations of these children gave negative results. The sources of their infection were not determined.
§ Chi square = ± 0.95 = 342 chances per 1,000.

sufficiently large to provide an approximate estimate of the general situation in the entire group of homes.

As the investigation continued, an increasing tendency was observed not only for partially surveyed groups to accept complete epidemiologic

study but also for the entire personnel of recently approached families to submit to Mantoux tests the first time this health measure was recommended. Apparently the educational influence of the program gradually facilitated its application.

Of the 733 parents who received the test at an average age of about 36 years, 57.3 per cent were found to be sensitive to tuberculin (table 2). Infection with tubercle bacilli had been introduced into this group at an average rate, therefore, of about 1.6 per cent annually.

The experience of the 860 tested children in these homes was definitely superior to that of their parents. At an average age of 6.3 years only 5.2 per cent of the former were found to be sensitive to tuberculin (table 2). The average annual rate of attack by primary infection for this group was 0.8 per cent, which is half the rate (1.6 per cent) recorded for the parents. These observations show that the risk of tuberculous infection recently faced by these children was distinctly lower than that experienced by their parents during preceding years and suggests that the risk of infection prevalent in the general environment had declined appreciably in the previous three decades.

The children included in this study were living in intimate contact with a liberally infected group of adults (57.3 per cent infected, table 2), but in spite of this exposure only 5.2 per cent had acquired sensitivity to tuberculin when an average of 6.3 years was reached. This observation provides circumstantial evidence to the effect that tuberculosis of the first infection type (this term is currently applied to the broad introductory phase of the evolution of the disease), which created the state of sensitivity to tuberculin in the adults, is not an effective source of contagion. In other words, tuberculosis in the primary stage of development does not seem to be an important source from which children acquire infection with tubercle bacilli.

Additional information relative to the households included in this study is revealed by the data in table 3. The observations on the partially surveyed units probably call for no discussion except mention of the fact that the incidence of sensitivity to tuberculin recorded for the tested senior and junior members of these homes approximates that noted for the corresponding age groups in the completely canvassed units. The general similarity in this respect between the partially and the completely surveyed households suggests that the observations made on the latter probably indicate with considerable accuracy the situation generally prevalent in the former.

According to the data in table 3 for the 213 completely tested households, neither parent was infected in 46 units (group 1), 1 parent was infected in 84 units (group 2) and both parents were infected in the remaining 83 units (group 3). Of the 77 children residing with adults whose reaction to the Mantoux test was negative (group 1), 5.2 per cent

were found to have positive reactions to tuberculin when tested at an average age of 5.4 years. Since the children of this group were living with uninfected parents, the tuberculous infections acquired by the former obviously were derived from sources outside the immediate family. For this sample of children living in tuberculosis-free homes, approximately 1 in 100 was infected annually from extraneous sources. This observation suggests that the primary infection risk or attack rate provided by the general extradomiciliary environment of children from Minneapolis homes of the type of which this series is representative amounts to roughly 1 per cent annually.

The incidence of sensitivity to tuberculin (4.8 per cent) observed for the 130 children from homes in which 1 parent was infected (group 2) closely approximates that (5.2 per cent) recorded for the children living with uninfected adults. This observation is interpreted as dependable evidence that the tuberculin-sensitive senior members of the homes included in group 2 were not serving as active sources of contagion and that the type of tuberculosis responsible for their specific allergy was not readily communicable. This deduction derives additional support from the observed failure of the 1 infected parent to contaminate the other adult in the home.

The incidence of sensitivity to tuberculin (11.3 per cent) recorded for the 133 children from homes in which 2 infected adults were present (group 3) is distinctly higher than that recorded for the junior members of the households in which 1 or neither of the parents was infected (groups 1 and 2, respectively). The value of chi square (1.48), computed from the data for the children in groups 1 and 3 (without making any correction for the disadvantage of a higher average age for the junior members of the latter group), indicates that the chances are 140 to 1,000 that the observed difference in the incidence of tuberculin-sensitive children in these 2 series of cases is the accidental result of random sampling. Apparently, no significant increase in infection among children attended the presence of 2 infected parents in each of the homes comprising group 3. This observation is interpreted as evidence that these contaminated adults, who were known to have primary tuberculosis by virtue of their demonstrated sensitivity to tuberculin, were not serving as active sources of contagion.

The data in the remaining section of table 3 for the completely surveyed homes show that the incidence of households with infected children was not significantly higher in the series of 83 units with 2 infected parents than it was in the group of 46 homes with no tuberculin-sensitive adult.

In general, the data in tables 2 and 3, from several angles of approach, agree in indicating that the first infection type, or the primary stage in the evolution of tuberculosis, the condition which is present in

each tuberculin-sensitive patient and actually created this special state of allergy, is a relatively unimportant source of human contact infections. Apparently, the disease must progress beyond the introductory or primary phase before it becomes a serious source of human contact infection. Since sensitivity to tuberculin is present in a high percentage of the senior members of the population, the observed failure of primary tuberculosis, per se, to serve as an important public menace to health is encouraging. Efforts to prevent human contact infection probably can be focused almost entirely on the identification and segregation of patients whose pulmonary disease has progressed beyond the primary, or first infection, stage of development.

The frequent presence of tubercle bacilli in the pharyngeal secretion and the gastro-intestinal contents of children with primary tuberculosis has created concern relative to the potential infection risk provided by the tuberculin-sensitive junior members of the population. Data pertaining to this question are provided by observations made on 121 children who entered the Lymanhurst Health Center uninfected and attended the school for various periods, throughout which they were in intimate daily contact with classmates who had primary tuberculosis, in most instances in the fibrotic or the calcified stage of development. The time of attendance at Lymanhurst averaged five months for 67 of the originally uncontaminated children, and during this period 3, or 4.5 per cent, became sensitive to tuberculin. The incidence of new primary infections for this series (4.5 per cent) was slightly higher than that (3.8 per cent) observed for the remaining 52 children, who spent an average of twenty-five months at Lymanhurst. The failure of the increase in infections to parallel the increase in the length of intimate contact with tuberculin-sensitive students is interpreted as evidence that children with primary tuberculosis in the fibrotic or the calcified stage are relatively unimportant sources of infection. If a readily communicable phase of tuberculosis of first infection exists, it probably is limited mainly to the early stage of the disease. The general failure, however, of the condition to produce an abundance of sputum and the customary tendency of children not to expectorate doubtless reduce the frequency with which children with primary tuberculosis of recent origin infect their associates. Furthermore, the communicability of this condition is probably diminished by the general tendency of these patients to discharge tubercle bacilli mainly by way of the intestines. Although the contagiousness of primary tuberculosis in various stages of development and for different age groups cannot be accurately estimated, it seems reasonable to believe that this condition falls far short of the ulcerative reinfection type of pulmonary tuberculosis as a public menace to health.

Additional details relative to the manner in which tuberculin-sensitive patients were distributed among the 213 completely tested households

are disclosed by table 4. The homes in which no infected child was present are separated in this table from those which included 1 or more contaminated children. This arrangement of the data shows that 42, or 19.7 per cent, of the thoroughly canvassed households did not contain a single tuberculin-sensitive member. In accordance with the economical plan for rating homes, these units were given an accredited status solely on the basis of the results of the Mantoux test survey. About 20 per cent of the total population of the entire series of completely surveyed units was living in an immediate environment of this character. In

TABLE 4.—*Additional Details Relative to the Completely Surveyed Groups of Household Units*

Group	Number of Infected Persons in Each Home: Parents	Number of Infected Persons in Each Home: Children	Number of Homes in Each Group	Percentage of Completely Surveyed Units	Personnel of Households in Each Group	Percentage of the Population in Each Group of Completely Surveyed Units	Basis on Which the Accredited Rating Was Founded
			Homes in Which No Infected Child Was Present				
1 A*	0	0	42	19.7	154	20.1	No infected person present in the home
2 A	1	0	78	36.6	275	35.9	Infected parent had not contaminated senior and junior associates
3 A*	2	0	71	33.3	251	32.8	Infected parents had not infected their children
Total			191	89.7	680	88.8	
			Homes in Which One or More Infected Children Were Present				
1 B	0	1	4	1.9	15	2.0	
2 B	1	1	6	2.8	23	3.0	
3 B	2	1	9	4.2	33	4.3	
3 C	2	2	3	1.4	15	2.0	
Total			22	10.3	86	11.2	

* The numeral refers to the group; the letter, to a subdivision of the group. Consequently, groups 1 A and 1 B = group 1 in table 3.

general, these observations demonstrate the existence in Minneapolis of tuberculosis-free households and suggest that the local incidence of homes in which this ideal situation prevails is encouragingly high. These observations also seem to indicate that the eradication of human tuberculosis is a practical problem the solution of which merely awaits a general intensification of present efforts to prevent infection in man by contact. Important progress in this direction, obviously, has already been accomplished in some localities.

Sensitivity to tuberculin was limited to the adult members of 149 families (groups *2A* and *3A*, table 4). In 78, or 36.6 per cent, of the 213 completely surveyed units only 1 parent was infected, and in 71, or 33.3 per cent, both parents were sensitive to tuberculin. Since the

1 infected parent in each home group 2*A* had not infected the remaining members of the family, and since the 2 tuberculin-sensitive adults in each home in group 3*A* had not contaminated their children, these 2 series of units were tentatively accredited, solely on the results of the Mantoux tests, with containing no person with open tuberculosis. Consequently, without incurring the expense of clinical, laboratory and roentgen examinations, a total of 191, or 89.7 per cent, of the 213 completely tested households were rated as safe units for children to live in. The economy

TABLE 5.—*Details Relative to the Completely Surveyed Household Units in Which Infected Children Were Present* *

Father	Roentgenogram	Mother	Roentgenogram	Children 1	2	3	4	5	Probable Source of Infection
Both Parents Uninfected									Group 1 B
M—R—		M—R—		M+R+					Unknown
M—R—		M—R—		M+R+					Unknown
M—R—		M—R—		M+R+					Unknown
M—R—		M—R—		M+R+†	M—R—	M—R—	M—R—		Aunt
One Parent Infected; Other Parent Uninfected									Group 2 B
M—R—		M+R+	Negative	M+R+					Unknown
M—R—		M+R+	Negative	M+R+					Unknown
M+R+	Negative	M—R—		M+R+	M—R—				Unknown
M+R+	Negative	M—R—		M+R+	M—R—				Unknown
M+R+	Negative	M—R—		M+R+	M—R—				Unknown
M—R—		M+R+	Negative	M+R+	M—R—	M—R—			Unknown
Both Parents Infected									Group 3 B and 3 C
M+R+	Negative	M+R+	Negative	M+R+					Unknown
M+R+	Negative	M+R+	Negative	M+R+					Unknown
M+R+	+‡	M+R+	Negative	M+R+§					Father
M+R+	Negative	M+R+	Negative	M+R+					Unknown
M+R+	Negative	M+R—	None	M+R+	M—R—				Unknown
M+R+	Negative	M+R—	None	M+R+	M—R—				Unknown
M+R+	Negative	M+R—	Negative	M+R+	M—R—				Unknown
M+R+	Negative	M+R—	Negative	M+R+	M—R—				Unknown
M+R+	Negative	M+R—	Negative	M+R+	M+R+				Unknown
M+R+	Negative	M+R—	Negative	M+R+	M—R—	M—R—			Unknown
M+R+	Negative	M+R—	Negative	M+R+	M+R+	M—R—			Unkonwn
M+R+	Negative	M+R—	Negative	M+R+	M+R+	M—R—	M—R—		Unknown

* M—R—, Mantoux test negative and no roentgen study made; M+R+, Mantoux test positive and roentgen study made; M+R—, Mantoux test positive and no roentgen study made.
† Child died of miliary tuberculosis at the age of 27 months.
‡ Father had phthisis.
§ Pneumonic infiltration in each lung and tuberculosis of right hip.

accomplished by this method of evaluating the home environment as satisfactory is obvious.

The second section of table 4 presents the records for the completely surveyed households which included tuberculin-sensitive children. Attention is called merely to the fact that the incidence of homes of this character was relatively low for each of the different groups of units and that it displayed no special relationship to the inclusion, in some instances, of infected parents.

A graphic representation of additional details relative to the thoroughly canvassed households which included tuberculin-sensitive children is provided by table 5. Clinical, laboratory and roentgen examinations

were made on all the 25 infected children and on 27 of the 30 infected adults living in these homes. As a result of the special study of these units, only 1 parent and 2 children were found in whom the disease had progressed beyond the primary stage. One of the latter (included in group 1*B*) apparently was infected by a tuberculous aunt, who visited the home for a short period. This deduction is supported by the observed absence of sensitivity to tuberculin from the remaining 5 members of the household. The infected child in this home died of miliary tuberculosis at the age of 2 years. The other child whose disease had progressed beyond the primary stage of development was exposed to a father with the reinfection, or adult, type of pulmonary tuberculosis (group 3*B*). Roentgen study of this child revealed bilateral pneumonic infiltrations and tuberculous involvement of the right hip. In this instance follow-up studies indicated that the pulmonary lesions probably were primary whereas the involvement of the bone was a secondary form or stage of the disease.

Although roentgen study was made of 26 additional tuberculin-sensitive adults who were residing with infected children, no additional sources from which the latter acquired their contamination were discovered. Apparently, most of these infections were extrafamilial in origin.

Details relative to 9 households represented in the survey by 1 parent and 1 or more children and in which infected children were present are shown in the first two sections of table 6. The first unit in this series was composed of 6 members. Although the father did not receive the Mantoux test, the fact that his wife and 3 of his children were uninfected is strong circumstantial evidence that he was not an active source of contagion. The 1 infected child had been exposed to a tuberculous aunt in 1926, during a short period in which the latter was awaiting admission to a sanatorium. The child had a positive Mantoux reaction shortly after this exposure, but roentgenograms of her chest repeatedly failed to reveal any evidence of disease. In 1931 she had slight hemoptysis, and a roentgenologic examination made at that time revealed a small cavity in the subclavicular region of the right lung.

The partial survey of the 8 homes where infected children were known to be living with at least 1 tuberculin-sensitive parent (second section of table 6) disclosed 2 fathers with phthisis. The source from which the remaining infected children acquired their infection was not determined.

The combined data for the 31 households in which one or both parents received the Mantoux test and in which infected children were present (tables 5 and 6) show that definite exposure of the children to an adult with phthisis occurred in 5, or 16.1 per cent, of these homes.

Included in this investigation were 8 additional households in which a parent with definite ulcerative pulmonary tuberculosis was present, but in these the parent had failed to contaminate his children (last section of table 6). Two of these tuberculous adults were carefully segregated at home, 3 were sent to sanatoriums and the remaining 3 received some form of collapse therapy and remained in the home.

TABLE 6.—*Details for Partially Tested Household Units from Groups 4 and 5 (Table 3) in Which Infected Children Were Present and for Units Which Included Adults with Open Tuberculosis Who Had not Infected Their Children**

Father	Roentgenogram	Mother	Roentgenogram	Children					Probable Source of Infection†
				1	2	3	4	5	
		One Parent Tested and Found Uninfected							Group 4, Table 3
		M—R—		M+R+‡	M—R—	M—R—	M—R—		Aunt
		One Parent Tested and Found Infected							Group 5, Table 3
		M+R+	Negative	M+R+					Unknown
		M+R+	Negative	M+R+					Unknown
		M+R+	Negative	M+R+					Unknown
M+R+	+			M+R+					Father
M+R+	+			M+R+	M—R—				Father
M+R+	Negative			M+R+	M—R—				Unknown
		M+R+	Negative	M+R+	M—R—				Unknown
		M+R+	Negative	M+R+	M+R+				Unknown
		Uninfected Children Living with Adults with Phthisis							Different Groups, Table 3
		M+R+	+	M—R—					Mother; home care for phthisis
M+R+	+	M+R+	Negative	M—R—					Father; in sanatorium
		M+R+	+	M—R—					Mother; extrapleural thoracoplasty
M+R+	+	M+R+	Negative	M—R—					Father; paralysis of the phrenic nerve
M+R+	+	M+R+	Negative	M—R—					Father; in sanatorium
M—R—		M+R+	+	M—R—					Mother; pneumothorax
M+R+	+	M+R+	Negative	M—R—	M—R—				Father; rest in bed at home
M+R+	Negative	M+R+	+	M—R—					Mother; in sanatorium

* M—R—, Mantoux test negative and no roentgen study made; M+R+, Mantoux test positive and roentgen study made; +, phthisis.
† Disposition of persons with open tuberculosis who had not infected their own children.
‡ Infected in 1926; phthisis developed in 1931.

At the conclusion of this preliminary survey, a total of 13 adults and 1 child with the reinfection, or adult, type of ulcerative pulmonary tuberculosis were known to be present as members or visitors in the 642 households included in the study. Eleven of these 14 patients with open tuberculosis were discovered by various clinics and physicians who were not participating directly in this investigation. In only 3 instances, therefore, can this preliminary survey be given exclusive credit for identifying previously undiagnosed phthisis. It led to the detection of

1 case in which the condition was suspected; necropsy showed that the patient had metastatic sarcoma of the lung. Although the recognition of 1 suspected and 3 definite victims of phthisis required 1,593 Mantoux tests and roentgen examinations of 70 tuberculin-sensitive members of households in which infected children were present, the immediate and ultimate benefits to be credited to the discovery of these potential and active human sources of contagion doubtless more than compensate for the expenditure of effort and funds their identification incurred.

The value of this preliminary survey is by no means limited merely to the discovery of a few menaces to the public health. In addition to its general educational influence, it established information relative to the distribution of infected persons among the members of a series of households, and this information should prove valuable when each group is rechecked. With this knowledge available, a future increase in the infected personnel of any of these homes can be detected easily, promptly and inexpensively; thus, subsequent surveys obviously will single out units in which a spread of tuberculosis is occurring and in which special examinations are imperative.

In view of its multiple benefits, the general application to commonly neglected social groups of an inexpensive method for identifying homes that harbor patients with open tuberculosis, which involves repeated household surveys by means of the Mantoux test and concentrates the use of the more expensive procedures, such as roentgen examinations, on the tuberculin-sensitive members of units that include infected children, is recommended. The promotion by physicians engaged in private practice of individual unsubsidized programs of this general character doubtless will materially aid present antituberculosis campaigns and simultaneously accelerate the eradication of tuberculosis of human origin. The use of an economical alternative for the preferred plan of more thoroughly canvassing household units probably should be limited mainly to fields in which a lack of funds leaves no alternative.

SUMMARY

An economical method for detecting households that harbor patients with open tuberculosis was used in this study. The method included the routine use of the Mantoux test but concentrated the use of the more expensive procedures, such as roentgen examinations, on the tuberculin-sensitive members of homes in which infected children were present. The economy accomplished in this manner seemed to make the plan suitable for general use in private practice.

In the preliminary survey 0.1 mg. of old tuberculin was administered to 1,593, or 69.1 per cent, of the 2,305 senior and junior members of 642 homes.

The investigation included the entire personnel of 213 households. Of the remaining 429 homes, 307 were represented in the survey by 1 parent and 1 or more children, and the remaining 122 units were represented solely by children.

The Mantoux test was applied to 57.3 per cent of the parents and to 83.9 per cent of the children in these homes.

Of the 733 parents who were tested at an average age of about 36 years, 57.3 per cent were sensitive to tuberculin. The annual rate of attack by primary infection for this group averaged about 1.6 per cent.

Of the 860 children who were tested at an average age of 6.3 years, 5.2 per cent were sensitive to tuberculin. The annual rate of attack by primary infection averaged about 0.8 per cent. Apparently the mean risk of infection recently faced by these children was distinctly lower than that experienced in preceding years by their parents. This observation indicates that exposure to open tuberculosis is experienced infrequently by children residing in Minneapolis homes of the type included in this study.

Various observations are presented which are interpreted as evidence that primary tuberculosis, the type or stage of the disease that is present in each tuberculin-sensitive patient, is a relatively unimportant source from which infection in man is acquired by contact. Apparently, efforts to control the human source of the disease can be concentrated almost exclusively on the identification and segregation of patients with the ulcerative or reinfection type of pulmonary tuberculosis.

Of the 213 completely surveyed households, 42, or 19.7 per cent, did not contain an infected member. These units were tentatively rated as certified, tuberculosis-free homes, solely on the basis of the results of the Mantoux tests.

In 149 of the 213 completely surveyed homes tuberculin sensitivity was limited to the adult members of the family. The observed failure of these infected parents to contaminate their children was accepted as evidence that the former had no readily communicable or open type of tuberculosis. Consequently, these households were tentatively accredited as contagion-free units, solely on the basis of the results of the Mantoux tests.

Merely by applying Mantoux tests and without incurring the expense of additional examinations, 191, or 89.7 per cent, of the completely tested units were tentatively rated as safe for children to live in. Retention of this accredited standing is deemed contingent on periodic demonstration by means of the Mantoux test that the number of infected persons is not increasing.

Infected children were present in only 10.3 per cent of the 213 completely surveyed households. The use of roentgenologic, clinical and

laboratory examinations was concentrated on the tuberculin-sensitive members of these units. The source from which infection with tubercle bacilli was probably acquired by the tuberculin-sensitive child was determined in only 2 of the cases in 22 homes.

At the conclusion of this initial survey, 14 patients with the ulcerative or adult type of pulmonary tuberculosis were known to be present in the entire group of 642 households. Eight of these persons had not infected their children, owing possibly to the early recognition of the disease and the subsequent observance of prophylactic measures.

This survey was responsible for the detection of only 3 of the 14 cases of open tuberculosis in the units surveyed. It led to the discovery of 1 case in which the condition was suspected and in which the diagnosis is still pending at the time of writing.

The economical method for tentatively determining whether households merit an accredited rating results in the identification of human spreaders of tubercle bacilli. It also establishes knowledge relative to the distribution of infected persons in the personnel of different units. This knowledge facilitates the recognition on subsequent surveys of homes in which the incidence of infected members is increasing. The economical method for canvassing homes also exerts a valuable educational influence on the laity. Its liberal use for the purpose of detecting human sources of contagion in social groups that otherwise would not be investigated is recommended.

INVESTIGATIONS ON HEMOPHILIA

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Three years ago one of us [1] reported on clinical and experimental investigations on two children with hemophilia and summarized the current ideas as to the cause of the abnormally prolonged coagulation time in that disease. Also, some experiments were reported regarding the existence of a substance promoting coagulation which should be present in normal plasma and serum and almost absent from the plasma and serum of patients with hemophilia. These experiments were based on the finding of Govaerts and Gratia,[2] which was confirmed and amplified, that normal plasma and serum when totally free from the coagulation ferment are able to accelerate coagulation, even in small concentration. Ultrafiltrates of normal plasma or serum do not have this influence. The substance which might be held responsible for the coagulation-promoting influence has been examined more closely. This article contains the results of the investigation and also those of the first clinical applications.

CHEMICAL STUDIES

To which protein fraction of the serum or the plasma does the coagulation-promoting substance show the greatest affinity?

One of us [1] found that the coagulation-promoting substance present in normal plasma and serum not only was nonultrafiltrable but was absent from the so-called protein-containing ultrafiltrate, i. e., an ultrafiltrate obtained by using a membrane with increased permeability.[1] Probably in agreement with this result is the fact that the coagulation-promoting substance was also found to be absent from ascites fluid. From these facts it was concluded that the coagulation-promoting substance must be present in the coarse-disperse protein fractions of the plasma.

The possibility of isolating separate protein fractions containing the coagulation-promoting product from the plasma or the serum was inves-

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1. van Creveld, S.: Sporadische haemophilie, Maandschr. v. kindergeneesk. **3**:351, 1934.

2. Govaerts, P., and Gratia, A.: Contribution à l'étude de l'hémophilie, Rev. belge sc. méd. **3**:689, 1931.

tigated in the first place by the method of precipitation,[3] certain concentrations of sodium sulfate being used. The precipitate was washed free from the remains of other substances of the plasma and was then dissolved in a quantity of physiologic solution of sodium chloride corresponding with the original quantity of plasma or serum. In this way we found that:

1. If fibrinogen and euglobulin are precipitated from normal plasma simultaneously (according to the method of Howe, with 14 cc. of a 14.5 per cent solution of sodium sulfate to 1 cc. of plasma), and the precipitate is treated in the aforementioned way, the solution obtained, which contains only fibrinogen and euglobulin, exerts a coagulation-

TABLE 1.—*Influence of Fresh Normal Plasma and of the Solution of Fibrinogen and Euglobulin Precipitated from This Plasma on the Coagulation Time of Hemophilic Plasma*

No. of Experiment	Added to Recalcified Oxalated Hemophilic Plasma	Dilution	Interval Before the Beginning of Coagulation, Minutes
	Normal plasma	1:5	15
	Normal plasma	1:25	20
	Normal plasma	1:125	30
I	Solution of fibrinogen and euglobulin from this plasma	1:5	12
	Solutoin of fibrinogen and euglobulin from this plasma	1:25	15
	Solution of fibrinogen and euglobulin from this plasma	1:125	23
	Physiologic solution of sodium chloride	1:5	70
II	Another normal plasma	1:5	15
	Physiologic solution of sodium chloride	1:5	90

promoting influence which is at least as strong as that of the plasma itself (table 1).

2. When the same reagent is added to serum, the solution obtained, which in this case contains euglobulin only, does not exert any coagulation-promoting influence (table 2).

From these experiments we concluded that the coagulation-promoting substance could be identical neither with the euglobulin nor with the fibrinogen itself, since normal serum has an even stronger coagulation-promoting activity than the corresponding plasma. The coagulation-promoting substance present in plasma and in serum is certainly not identical with and is probably not adherent to the euglobulin. Tables 1 and 2 show, further, that fresh normal plasma and serum even when highly diluted exert their coagulation-promoting influence. The limit of the activity is found with a dilution of about 1:125.

3. (*a*) Bendien, W. M., and van Creveld, S.: Investigations on Haemophilia, Maandschr. v. kindergeneesk. **5**:179, 1936; abstr., Acta brev. Neerland. **5**:135, 1935.

About the origin of the coagulation-promoting substance, the following comments may be made. The current idea is that in hemophilia one is dealing with an abnormal stability of the blood platelets. According to our opinion the cause of this abnormal stability must be sought not in an abnormal structure of the blood platelets but in the absence of an unknown factor from the hemophilic plasma. If in hemophilia one were dealing only with an abnormal structure of the blood platelets, hemophilic serum would not differ in any point from normal serum.

TABLE 2.—*Influence of Fresh Normal Serum and of the Solution of the Euglobulin Precipitated from this Serum on the Coagulation time of Hemophilic Plasma*

No. of Experiment	Added to Recalcified Oxalated Hemophilic Plasma	Dilution	Coagulation Time, Minutes	
			Beginning	Completion
I	Normal serum	1:5	..	20
	Normal serum	1:25	..	29
	Solution of euglobulin from this serum	1:5	55	90
	Solution of euglobulin from this serum	1:25	55	100
	Physiologic solution of sodium chloride	1:5	60	110
II	Normal serum	1:5	..	10
	Normal serum	1:10	..	13
	Normal serum	1:20	..	22
	Normal serum	1:40	..	28
	Normal serum	1:80	..	35
	Solution of euglobulin from this serum	1:5	..	40
	Solution of euglobulin from this serum	1:25	..	45
	Physiologic solution of sodium chloride	1:5	..	50
III	Normal serum	1:5	5	7
IV	Normal serum	1:5	6	8
V	Normal serum	1:5	5	8
VI	Normal serum	1:5	4	9
	Normal serum	1:10	6	20
	Normal serum	1:25	10	35
	Normal serum	1:50	16	45
	Normal serum	1:125	30	55
	Normal serum	1:250	35	..
	Physiologic solution of sodium chloride	1:5	35	..

In the process of coagulation, however, the hemophilic serum would be formed more slowly. In reality, a difference does exist. Hemophilic serum exerts hardly any coagulation-promoting activity on hemophilic plasma, which is in great contrast to the effect of normal serum (table 3). Therefore, in hemophilic serum a certain substance must be lacking.

The coagulation-promoting substance does not appear to be identical with the coagulation ferment. We were able to confirm the observation of Bordet [4] and of Govaerts and Gratia [2] that when normal plasma is

4. Bordet, J.: Considérations sur les théories de la coagulation du sang, Ann. Inst. Pasteur **34**:561, 1920.

freed from the substances of the coagulation ferment by treatment with calcium phosphate $Ca_3(PO_4)_2$ or by infiltration through a Pasteur-Chamberland candle it is no longer able to coagulate but can still exert a coagulation-promoting activity on hemophilic plasma.

Schmitz [5] drew attention to a method of Mallenby by which two kinds of fibrinogen can be precipitated from horse's plasma, real fibrinogen and so-called coagulation globulin. We [3] investigated whether the last-mentioned fraction is also present in serum. Indeed, it appeared that by feebly acidifying serum with acetic acid to a p_H of about 5.5 after a tenfold dilution with distilled water, a protein fraction could be precipitated. This fraction was washed with distilled water and then

TABLE 3.—*Influence of the Precipitate (with Normal Acetic Acid) from Fresh Normal Plasma and from Fresh Normal Serum as Compared with That of the Precipitate from Hemophilic Plasma and from Hemophilic Serum on the Coagulation Time of Hemophilic Plasma*

No. of Experiment	Added to Recalcified Oxalated Hemophilic Plasma	Dilution	Coagulation Time, Minutes	
			Beginning	Completion
I	Normal plasma	1:5	8	10
	Solution of the precipitate from this plasma	1:5	3	5
	Solution of the precipitate from this plasma	1:25	8	12
	Normal serum	1:5	6	9
	Solution of the precipitate from this serum	1:5	3	9
	Solution of the precipitate from this serum	1:25	13	21
	Physiologic solution of sodium chloride	1:5	29	35
II	Solution of precipitate from hemophilic plasma	1:5	35	50
	Hemophilic serum	1:5	28	40
	Solution of precipitate from hemophilic serum	1:5	25	35
	Physiologic solution of sodium chloride	1:5	40	50

dissolved in a quantity of saline solution (0.9 per cent) corresponding to the volume of serum from which it was obtained. Remarkably, this solution when added to hemophilic plasma or blood exerted a coagulation-promoting activity which was about the same as that of the serum from which the product was prepared (table 3). From this we concluded that about all the coagulation-promoting substance which was present in the serum was also present in the solution.

A protein fraction of about the same concentration (about 5 per cent) could be precipitated from hemophilic plasma and serum. However, this fraction, after being dissolved, showed hardly any coagulation-promoting influence on hemophilic plasma and on hemophilic blood (table 3). From this we concluded that the precipitated protein itself does not promote coagulation. We are justified, however, in saying that

5. Schmitz, A.: Ueber Fibrinogen und ein gerinnungsförderendes Plasmaglobulin, Ztschr. f. physiol. Chem. **222**:155, 1933.

the coagulation-promoting substance is precipitated from normal serum together with the coagulation globulin.

Next we tried to obtain the coagulation-promoting substance in a more protein-free solution by physical methods.

For this purpose we [3] made use of the method of adsorption and elution, according to the principle of Willstätter. We adsorbed by means of norit. It appeared to be possible to adsorb practically all the coagulation-promoting substance from serum by a charcoal preparation. The great difficulty was the problem of the elution, i. e., how to set the adsorbed substance free again. In the beginning we tried a physiologic solution of sodium chloride for this purpose. When the charcoal to which the proteins were adsorbed was shaken for a long time with this solution, the greater part of the adsorbed proteins was freed. These eluates, however, appeared to be unable to promote the coagulation of hemophilic plasma; so the coagulation-promoting substance had remained adherent to the norit. Later, in using the principle of the so-called superseding adsorption with a surface active substance, we succeeded in freeing the coagulation-promoting substance from the charcoal with sodium desoxycholate.

In this way we could obtain part of the coagulation-promoting substance adsorbed to the norit in a medium poor in protein (the concentration of which was less than 1 per cent). These eluates had a low protein content and were free from cholesterol and lipoid phosphorus. In ultrafiltrating them we could even increase their content of coagulation-promoting substance, but the concentration of proteins increased also.

The practical disadvantages of the application of this method were that the loss of coagulation-promoting substance was still too large and that the whole treatment took too long a time because of the thermostability of the coagulation-promoting substance.

We have not yet been able to establish the chemical nature of the coagulating-promoting substance.

When coagulation globulin obtained from serum by means of the acidifying method previously mentioned is dissolved in physiologic solution of sodium chloride the smallest volume in which all the coagulation globulin can be dissolved is about one third of the volume of the serum from which the product was prepared. This volume is usually too large for ordinary injection. We found that by adding 3 or 4 per cent of sodium carbonate to the physiologic solution of sodium chloride the same quantity of coagulation globulin could be dissolved in a much smaller volume of sodium chloride (three times as small). Furthermore, it appeared that physiologic solution of sodium chloride, though it is the best medium for an eventual intramuscular injection (because it is isotonic), is not absolutely necessary for dissolving the coagulation globulin. A 3 or 4 per cent watery solution of sodium carbonate can also be used for dissolving the coagulation globulin in a small quantity of fluid. The p_H of this solution is from 8 to 8.5. When the p_H becomes too high, the coagulation-promoting activity decreases greatly. Furthermore, it is of great importance that in the preparation of the coagulation

globulin nonlipemic serum be used (obtained by taking blood from patients—as a rule patients with high blood pressure—who are fasting). When the serum taken is lipemic, the solutions of coagulation globulin obtained are opalescent to a certain degree, even after filtration through a Berkefeld filter, and this is an undesirable condition, especially if the product is to be injected intravenously.

When the solution is to be ingested orally, one can prepare the product from the serum of animals, e. g., cow's or horse's serum.

The concentrated solution obtained (the coagulation globulin being dissolved in about one tenth of the volume of the serum from which

TABLE 4.—*Influence of a Fresh Solution of Coagulation Globulin and of Fresh Serum on the Coagulation Time of Recalcified Oxalated Hemophilic Plasma*

Dilution of substance added	1:5	1:25	1:50	1:125	1:250
	Coagulation Time, Minutes				
Fresh coagulation globulin	½-3	1½- 5	2½-10	5-15	10-25*
Fresh serum	3-5	6 -15	10-25	20-35*	

Hemophilic plasma itself did not show any coagulation after thirty minutes

* No completion of the coagulation occurred.

TABLE 5.—*Stability of the Activity of the Solutions of Coagulation Globulin, Demonstrated by Their Influence on Hemophilic Plasma*

Dilution of coagulation globulin added to hemophilic plasma	1:5	1:10	1:25	1:50	1:125
	Coagulation Time, Minutes				
Fresh coagulation globulin	2-4	3-7	5-11	7-20	14-30
Coagulation globulin one week old	3-7	4-12	7-22	20-35*	35-
Coagulation globulin three weeks old	6-15	10-25	15-35*		

* No completion of the coagulation occurred.

it has been prepared) is highly active in vitro, much more so than the fresh serum itself. This was shown by an experiment in which a fresh solution of coagulation globulin and fresh serum were added separately in varying dilutions to recalcified oxalated hemophilic plasma. The times for the beginning and the completion of coagulation (at room temperature), expressed in minutes, are shown in table 4.

A highly important property of the solutions of coagulation globulin is that they keep their activity much longer than does the serum itself. This property is illustrated by the data in table 5.

When coagulation globulin was kept in a refrigerator for a week, its activity, which originally was twice that of fresh serum, was halved (table 5), but at that time the serum itself was no longer active. After

three weeks in the refrigerator, the activity of the coagulation globulin had diminished to one sixth of its original value.

We also examined the activity of the coagulation globulin on hemophilic blood to which we had added nothing to keep it fluid. For hemophilic blood at room temperature we found a coagulation time of seventy-five minutes. The addition of fresh coagulation globulin in a relation of 1 : 10 caused this blood to coagulate in from one and a half to three minutes. (One should remember, moreover, that addition to blood in a relation of 1 : 10 must be compared with addition to plasma in a relation of 1 : 5.)

CLINICAL APPLICATIONS

It is a well known fact that the prolonged coagulation time constantly present in cases of hemophilia can be decreased by the intravenous injection of normal blood or fresh serum. The effect of normal blood and serum has recently been studied by Patek and Stetson.[6] As the solutions of coagulation globulin obtained by us from serum in vitro had a much higher coagulation-promoting effect in a much smaller volume than the serum itself and were much more stable, the question arose as to how significant these preparations are clinically.

In considering how to give the preparations of coagulation globulin to patients with hemophilia, we thought in the beginning that we could not expect any effect from oral administration, though this method has great advantages. Only in a later stage of our research did we give our products orally, and then we did so largely because of recent experiments in America, the starting point of which, however, was quite different from that of ours.

Eley and his co-workers[7] reported an investigation on the activity of a coagulation-promoting extract prepared from human placentas in patients with hemophilia. The placentas were from women who did not have syphilis and had not had toxicosis during pregnancy. The product obtained, which was brown and opaque, had a strong coagulation-promoting activity and was given orally or intramuscularly to fifteen patients with hemophilia, generally with satisfactory results.

Our experience with the oral administration of the coagulation globulin prepared from serum was generally not so favorable as that of Eley and his co-workers.

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6. Patek, A. J., and Stetson, R. P.: Hemophilia: I. The Abnormal Coagulation of the Blood and Its Relation to the Blood Platelets, J. Clin. Investigation **15**:531, 1936.

7. Eley, R. C.; Green, A. A., and McKhann, C. F.: The Use of a Blood Coagulant Extract from the Human Placenta in the Treatment of Hemophilia, J. Pediat. **8**:135, 1936.

The first patient to whom we gave the product orally was a boy 3 years old with sporadic hemophilia (G.) who had previously been described by one of us.[1]

Coagulation of his blood at room temperature began at one hour and ended at two hours, as it had formerly done.[8] One hour after the ingestion of 60 cc. of a solution of coagulation globulin, prepared from 500 cc. of cow's serum (about 1.25 liter of cow's blood), the coagulation time was again determined. The values for the beginning and the completion of coagulation were twenty-five and forty-five minutes, about half those for the original coagulation time. Three days later the values were thirty and sixty minutes.

Keeping in mind that the normal coagulation time at room temperature is twelve and sixteen minutes, coagulation occurring rather quickly, we cannot say that our boy's coagulation time had become normal, though it had obviously shortened and the clinical condition had apparently improved.

The same child repeatedly took an analogous product orally, in one instance the same type of product prepared from human serum. He was treated as an ambulant patient. After he had taken the product he always complained of a slight headache, which soon disappeared. According to his mother he was always in good condition for some time after he had taken the solution. Though he fell repeatedly, he did not get any hemorrhagic spots. One month after the last ingestion of the products he again had a hemorrhage, and his coagulation time appeared to be the same as it had been before the administration of the solutions, i. e., one and two hours.

We also gave a solution of coagulation globulin (prepared from 600 cc. of fresh cow's serum) orally to a boy aged 12 with hemophilia (O.). The values for the coagulation time at room temperature before ingestion of the solution were one and one and three-fourths hours; six hours after ingestion they were thirty-five and seventy minutes, about half of the original values. Two days later, when we determined the coagulation time again, it had risen to one and one and three fourths hours; so the effect had disappeared. With further oral administration of solutions of coagulation globulin prepared from animal or human serum we obtained analogous results.

In a third patient with hemophilia, a boy 10 years old (Z.), sometimes no effect at all was seen from the oral administration of the product.

Summarizing, we seem to be justified in concluding that with the oral administration of coagulation globulin prepared from serum we sometimes obtained a favorable but unsatisfactory effect.

At the time of writing we are checking the results obtained by Eley and his co-workers,[7] especially those with the oral administration of a product prepared from the placenta, since this method of administration remains the safest.

In the meantime, we continued our intramuscular injections. A short description of our experience with this method follows.

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8. We always determined the coagulation time (in triplicate) of our patients with blood obtained by venous puncture. We considered the coagulation complete when the surface of the blood, after the test tube was cautiously turned, did not break.

Patient O. was given an intramuscular injection of 10 cc. of coagulation globulin prepared from 100 cc. of human serum. The coagulation time at room temperature before injection was fifty-five and one hundred and twenty minutes; six hours after the injection it was thirty and sixty-five minutes, nearly half of the original values. Several weeks later the same patient received an intramuscular injection of 20 cc. of coagulation globulin prepared from 200 cc. of human serum. The coagulation time of the venous blood before injection was one and one-fourth and two and one-half hours; six hours after the injection it was one-half and one hour, a little more than half of the original values. Two days later the results were three-fourths and one and three-fourths hours, so the effect had largely disappeared. When we determined the coagulation time at 37 C. the values also decreased to less than half and the effect also lasted for only a short time.

With our hemophilic boy of 10 years, Z., we could obtain the same results by the intramuscular injection of a product prepared from human serum.

After having obtained these results, which from a therapeutic point of view were also unsatisfactory, we proceeded, after careful examination, to intravenous injection.

This method we applied in the case of a boy 15 years old with hemophilia (B.) who generally had a moderately prolonged coagulation time. Before injection it was thirty and forty-five minutes at room temperature and twelve and seventeen minutes at 37 C. Sixteen cubic centimeters of coagulation globulin prepared from 200 cc. of human serum was divided in two parts and injected intravenously on two successive days. Six hours after the first injection the coagulation time was seventeen and twenty-six minutes at room temperature and five and eight minutes at 37 C. The normal values for the coagulation time of venous blood at 37 C. with our method are four and seven minutes. By this injection, therefore, we succeeded in bringing the coagulation time of this boy almost within the normal limits.

Next day his coagulation time was twenty-two and thirty minutes at room temperature and ten and thirteen minutes at 37 C.; so the effect of the injection given the day before had largely disappeared. We then injected intravenously the second half of the solution of coagulation globulin. Shortly afterward the coagulation time at 37 C. was six and nine minutes, which shows a clear effect. After one day the values were seven and eleven and one-half minutes and after two days eight and one-half and twelve minutes; they then remained about the same for some days.

Six weeks after the last injection, which was given during a period of hemorrhages, this patient, B., was given an injection of about 18 cc. of coagulation globulin prepared from 220 cc. of human serum. Before the injection the values for the coagulation time were seven and one-half and twelve and one-half minutes at 37 C. Because of the danger of an anaphylactic reaction (though we injected a product prepared from human serum) we injected 1 cc. intravenously one hour before we injected the other 17 cc. After about forty minutes a slight anaphylactic reaction occurred (headache and slight elevation of the temperature). Half an hour later it had disappeared. The coagulation time next morning, about eighteen hours after the injection, was eight and fourteen minutes at room temperature and three and one-half and six minutes at 37 C.; the time at which coagulation began had become normal, although completion of the coagulation, which in normal subjects occurs fairly suddenly, took several minutes.

One day later we found the coagulation time to be twelve and eighteen minutes at room temperature and four and one-half and eight minutes at 37 C.; so it was still shortened. Two days later the values were fourteen and twenty-two minutes at room temperature and six and nine minutes at 37 C. Four days later they were sixteen and twenty-eight minutes at room temperature and seven and eleven minutes at 37 C., the effect having entirely disappeared.

The effect of this injection could be clearly observed for between two and three days.

With this patient, who had a moderately prolonged coagulation time, we succeeded in keeping the values within the normal limits for about two days. While the coagulation time was normal, no new hemorrhages occurred.

To the 12 year old boy, O., previously mentioned, to whom we had given intramuscular injections of a solution of coagulation globulin, we now gave such a solution intravenously. The first time he received 10 cc. prepared from 100 cc. of human serum. It was interesting that no symptoms of anaphylaxis occurred at that time. A slight elevation of the temperature took place in the evening, but it soon disappeared.[9] The coagulation time at room temperature before the injection was one and one-fourth and two and one-fourth hours[10] and fifteen minutes after the injection three-fourths and one and one-fourth hours. In this experiment we thus observed a slight shortening of the coagulation time.

One week later the same patient was given an injection of 10.5 cc. of coagulation globulin prepared from about 100 cc. of human serum. This solution in vitro showed great activity. (This may appear from the fact that addition of this solution to hemophilic plasma in dilutions of 1:5 and 1:10 caused coagulation immediately after recalcification. Further, it appeared that in a dilution of 1:150 it showed an activity which equaled that of fresh serum in a dilution of 1:25). The patient's coagulation time at 37 C. before injection was fifty and ninety-five minutes. Ten minutes after the injection it was twenty-eight and sixty minutes; six hours after it was twenty-three and fifty minues, and twenty-four hours after it was eighteen and forty minutes. The coagulation time had therefore decreased to less than half its original length.

Five days later this patient had another injection of coagulation globulin, which also had no disagreeable consequences with the exception of a slight elevation of the temperature in the evening. This time he was given intravenously 11 cc. of a solution prepared from about 100 cc. of serum. The coagulation time at 37 C. before the injection was seventy-six and one hundred and thirty minutes. Ten minutes after the injection it was thirty-two and seventy-eight minutes; six hours after it was twenty-five and fifty-seven minutes, and twenty-four hours after it was twenty and forty minutes. The coagulation time had therefore decreased to less than one third of the original length.

It was remarkable that three days after the injection the coagulation time still appeared to be greatly decreased; it was seventeen and thirty-three minutes, less than one fourth of the original length. However, three days later it was thirty-five and seventy-five minutes. The patient was then given 13.5 cc. of a solution

9. This patient was probably suffering from chronic appendicitis, but because he was also suffering from hemophilia no operation could take place. This explains the moderate rise in temperature which he occasionally showed.

10. All determinations were performed in triplicate.

prepared from about 120 cc. of human serum. The coagulation time at 37C. twenty-four hours after the injection was fifteen and thirty-five minutes, and forty-eight hours after the injection, it was thirty-five and seventy-five minutes, so that the effect of this injection lasted for a much shorter time than that of the previous injection.

Several days later the patient was given 10 cc. of a solution prepared from 115 cc. of serum. The coagulation time at 37 C. before the injection was thirty-five and eighty-five minutes. Fifteen minutes after the injection it was thirty and seventy minutes; six hours after it was fifteen and thirty minutes; twenty-four hours after it was seventeen and forty minutes; two days after it was twenty-five and fifty-eight minutes, and three days after it was thirty-three and seventy minutes.

The effect of this injection was greatest six hours after the injection. After twenty-four hours it had diminished, and after three days it had practically disappeared.

From the series of experiments with this patient we seem to be justified in concluding that it is possible to shorten his coagulation time considerably by means of intravenous injections. The diminution was more pronounced than that obtained by oral administration or intramuscular injection of the preparation. However, we did not succeed in reducing the coagulation time to within normal limits.

For a definite explanation of the significance of the results obtained by us, the following points are of interest:

1. The so-called spontaneous remissions which sometimes occur in a patient with hemophilia, that is, the shortening of the coagulation time which may take place, especially after a period of serious hemorrhages. However, during the period in which we observed our patient O., the values for his coagulation time except after an injection were always between one and one-fourth and two hours when determined at 37 C. The diminution of his coagulation time after the injections to about one-half hour can thus be ascribed with certainty to the activity of our preparation.

2. The moment after the injection in which the effect was maximal and the duration of this effect. It is striking that the maximal effect does not occur shortly after the injection, when one accepts the homogeneous mixing of the blood. One can imagine that the effect of the activity in the circulating blood requires some time to reach its maximum. In patient O. we found three times that the effect was pronounced six hours after the injection, much more distinct than it was from ten to fifteen minutes after. Twice it appeared that twenty-four hours after the injection the effect was still greater than it had been six hours after the injection; another time it had somewhat decreased after twenty-four hours. The fact that twenty-four hours after the injection the effect in patient O. was always demonstrable is in accordance with the results of the injections in patient B, who had only a moderately increased

coagulation time. As to the duration of the effect of the injections, it showed great irregularity in our patient O., who had severe hemophilia.

3. The question as to how far the results obtained should be considered as a specific consequence of the solution administered or as the consequence of a nonspecific protein therapy. Opposed to the latter conception is the fact that for the injections we always used products prepared from human serum. Furthermore, we want to stress the great activity of our products when used in coagulation experiments in vitro, even in dilutions corresponding to those which occurred in the blood after the injection of the solutions (table 4).

Further, we know that with unspecific protein therapy the temperature always rises and there is a change in the concentration of the plasma proteins (protein spectrum) in the direction of an enlarged value for the coarse-disperse proteins (globulin and fibrinogen). Therefore we made a protein spectrum of the blood of our patient O. on two occasions, the first being six hours after an injection, when his coagulation time had greatly diminished and he showed a moderate elevation in temperature, and the second, when his coagulation time was prolonged, as usual, and he showed a slight elevation in temperature caused by another factor (his chronic appendicitis?). The first, when the coagulation time was fifteen and thirty minutes at 37 C., showed total protein 72.1 per cent, albumin 38.9 per cent, globulin 30.1 per cent (normal, from 18 to 24 per cent) and fibrinogen 4 per cent (normal, from 2.5 to 3.7 per cent). The second, when the coagulation time was thirty and seventy minutes at 37 C., showed total protein 71.8 per cent, albumin 36 per cent, globulin 31.6 per cent and fibrinogen 4.2 per cent. Practically, the protein spectrum had remained the same.[11] This is a strong argument in favor of the conception that the effect on the coagulation produced by our injections was not a nonspecific effect of the proteins.

In continuing our research we want to try by oral or by intravenous administration of the coagulation-promoting substances to reduce the coagulation time of patients with severe hemophilia to within the normal limits and to maintain this reduced coagulation time.

SUMMARY

The fact that in normal fresh plasma and serum a substance is present which exerts a coagulation-promoting influence on hemophilic plasma and blood is discussed.

The question of to which protein fraction of the serum or the plasma this substance shows the greatest affinity is discussed. Though the substance must be present in the coarse-disperse protein fraction, it undoubtedly is not euglobulin itself.

11. The increased globulin content of this patient had already been observed three years previously.

A method is described for precipitation of the coagulation-promoting substance from normal fresh serum by slight acidifying.

A simpler method is also described, i. e., adsorption and elution, by which the coagulation-promoting substance can be obtained from fresh normal serum in a medium poor in proteins.

By dissolving the coagulation globulin (which was precipitated from the serum by slight acidifying) in water or in physiologic solution of sodium chloride to which has been added 3 or 4 per cent of sodium carbonate, it can be dissolved into a volume which is ten times as small as the volume of the normal serum from which it has been prepared. This solution is free from cholesterol and lipoid phosphorus.

The solutions as obtained by the method described showed an activity which was about five times as great as that of the fresh serum itself. Moreover, these solutions remained active much longer than the serum itself when kept in the refrigerator.

The results obtained with oral, intramuscular and intravenous administration of solutions of the coagulation-promoting substance to three patients with hemophilia are described. Especially by application of the intravenous method distinct results were obtained. In one patient we succeeded repeatedly in keeping the coagulation time within normal limits for some days by an intravenous injection.

STABILIZING EFFECT OF INCREASED VITAMIN B (B_1) INTAKE ON GROWTH AND NUTRITION OF INFANTS

BASIC STUDY

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DETROIT

New standards have been set during the past few years for the growth of normal infants, owing to the increased knowledge of the nutritional requirements of babies during the first year of life. Such standards are expressed in terms of weight and height for age. The betterment of growth in these two directions has been due to numerous causes, not the least of which is the optimal intake of the dietary essentials and accessory food factors. McCollum and Simmonds,[1] however, presented evidence in their monograph to show that the great majority of children, both in the United States and in other countries, do not make the growth that might be expected in view of the developments in the science of nutrition.

In regard to vitamin B, a considerable amount of literature tends to show that while gross lack of this substance is encountered rarely in this country, evidence is seen frequently of moderate deficiency. The dietary habits, combined with the ever growing awareness of the nutritive essentials to health and growth, are such that there is small need to consider the grim conditions resulting from a diet completely deficient in vitamin B. Many of the symptoms arising from this complete lack, however, can be observed in a milder form in the every day debilities and illnesses of adults and children. A suboptimal intake of vitamin B

From the Research Laboratory of the Children's Fund of Michigan and the Children's Hospital.

This report is the first of a series that was stimulated by the late Prof. Lafayette B. Mendel, of Yale University, on the effect of augmented intakes of various supplemental foods on the growth, development and nutrition of infants. The expenses were defrayed in part by a grant from the Borden Company, through Mr. L. J. Auerbacher.

1. McCollum, E. V., and Simmonds, Nina: The Newer Knowledge of Nutrition, ed. 3, New York, The Macmillan Company, 1925.

may lead to ill defined functional disorders, anorexia, inefficient utilization of nutrients, a lowered hemoglobin content and even definite clinical symptoms. Hoobler,[2] in his picture of infantile beriberi in the Philippine Islands, described the effect of complete deficiency of vitamin B. He noticed not only marked nervous disabilities, such as stiffness of the neck, arms and legs, but profound degenerative changes in the digestive system. The latter persisted for some time after the nervous phenomena, which quickly disappeared when the antineuritic substance was added to the diet. This picture of infantile beriberi is particularly enlightening when attempts are made to understand the effects on growth, development and nutrition of a partial deficiency of vitamin B.

Karr[3] concluded that there is some relationship between the desire to partake of food and the amount of vitamin B in the diet. In animals, Cowgill[4] emphasized the importance of anorexia as a fairly early symptom of withdrawal of this substance from the diet. For example, in dogs, when the previous level of vitamin B in the diet had been high, anorexia developed in an average of twenty-one days. Dennett[5] and Bartlett[6] suggested that a lack of vitamin B may be an important factor in cases of anorexia in infants and that it tends to reduce resistance to infection.

Perhaps it is reasonable to suppose that vitamin B, in addition to stimulating the appetite, brings about better assimilation and utilization of food and so builds up the general tone of the body. Gaynor and Dennett[7] observed that the addition of vitamin B in the form of rice polishings to a dried milk formula resulted in a greater metabolic efficiency, which result could be attributed only to the augmented intake of vitamin B. The essence of their conclusion was that the infants receiving a vitamin B supplement grew better on an average daily intake of 35 calories per pound (0.5 Kg.) of body weight than the control infants on from 45 to 55 calories. Furthermore: "While weight in itself may be a poor standard for determining the effectiveness of vitamin B in infants, there being many methods of making a child gain, still it is a practical method of recording an infant's well-being." They

2. Hoobler, B. R.: Symptomatology of Vitamin B Deficiency in Infants, J. A. M. A. **91**:307 (Aug. 4) 1928.

3. Karr, Walter G.: Some Effects of Water-Soluble Vitamine upon Nutrition, J. Biol. Chem. **44**:255, 1920.

4. Cowgill, George R.: The Vitamin B Requirement of Man, New Haven, Conn., Yale University Press, 1934.

5. Dennett, R. H.: Routine Use of the Vitamin B Factor in Infant Feeding, J. A. M. A. **92**:769 (March 9) 1929.

6. Bartlett, W. M.: An Analysis of Anorexia, Am. J. Dis. Child. **35**:26 (Jan.) 1928.

7. Gaynor, M. F., and Dennett, R. H.: Rice Polishings as a Source of Vitamin B Complex in Infant Feeding, J. Pediat. **4**:507, 1934.

also found that anorexia, colic and lesions in the skin and mucous membranes were absent, that pallor was less and that the physical developments, e. g., crawling and teething, were more advanced in their experimental than in their control group.

Cowgill,[8] in discussing vitamin B_1 in relation to the clinic, said: "During the first six months of its life, the human subsists almost entirely upon milk and is therefore in the category of individuals who live on a restricted dietary." It has been demonstrated that cow's milk and in some instances breast milk do not contain the optimal quantity of vitamin B and that the infant given one of these foods may be receiving less than the minimal amount of vitamin B.[9] In fact, Cowgill quoted Ohta as stating that of 430 infants with beriberi in the clinics of Tokyo, 414 were breast fed. Dennett [5] advocated the addition of some accessory vitamin B factor "as a routine to the food of all bottle fed babies, just as cod liver oil and orange juice are universally used." Moore and Brodie,[10] in their studies on the effect of the diet during pregnancy, stated that "diets restricted by poverty, pernicious vomiting, diabetes or other causes need careful scrutiny from the standpoint of vitamins." More interest is being centered on the nutritional state of the gravid mother and the reflection of it on the offspring. During pregnancy, owing to the increased metabolism caused by the growth of the fetus, a diet which is on the threshold regarding its vitamin B content may become inadequate.

Subsequent to the observations by Morgan and Barry [11] on undernourished school children, Summerfeldt,[12] using one group of normal children as controls, fed another series of children a cereal mixture enriched with vitamin B and minerals. Because there were two variables in this experiment, either of which might have accounted for the gain in weight, Ross and Summerfeldt [13] later observed three groups of orphange children over a period of six months. These were given, respectively: (1) the regular diet of the orphanage, (2) the same diet

8. Cowgill, George R.: Vitamin B_1 in Relation to the Clinic, J. A. M. A. **98**:2282 (June 25) 1932.

9. Macy, I. G., and Outhouse, J. P.: Vitamin Content of Milk Used in Infant Feeding, Am. J. Dis. Child. **37**:379 (Feb.) 1929.

10. Moore, C. U., and Brodie, J. L.: The Relation of the Maternal Diet to Hemorrhage in the New-Born, Am. J. Dis. Child. **34**:53 (July) 1927.

11. Morgan, A. F., and Barry, M. M.: Underweight Children: Increased Growth Secured Through the Use of Wheat Germ, Am. J. Dis. Child. **39**:938 (May) 1930.

12. Summerfeldt, P.: The Value of an Increased Supply of Vitamin B_1 and Iron in the Diet of Children, Am. J. Dis. Child. **43**:284 (Feb.) 1932.

13. Ross, J. R., and Summerfeldt, P.: Value of Increased Supply of Vitamin B_1 and Iron in the Diet of Children, Am. J. Dis. Child. **49**:1185 (May) 1935.

plus a vitamin B concentrate made from wheat germ and yeast (free from iron) and (3) the same diet plus 3 ounces (85 Gm.) of a special cereal enriched with vitamin B and minerals. The third group showed an increase in the rate of growth and in the hemoglobin content. It should be noted that these observations were made on institutional children past infancy.

Few controlled studies have been carried out to determine the relation of nutrition to functional disorders. Those that have been made have produced conflicting reports regarding mental ability. For example, Maurer and Tsai [14] found a diminished capacity for maze learning when there was a lack of vitamin B in the diet of nursing rats, and this finding was confirmed by Bernhardt.[15] With mature rats however, Anderson and Smith [16] found that diets deficient in vitamin B did not alter their ability for maze learning. With Chicago children from 5 to 9 years of age, Balken and Maurer [17] observed that an adequate diet following a prolonged period of vitamin B deficiency produced rapid improvement in the performance of every child as tested by several standardized mental tests. The intelligence quotients of public school children were correlated with their diets in infancy by Hoefer and Hardy,[18] who found that those who ranked last had been breast fed for from four to nine months.

With the exception of the work of Gaynor and Dennett,[7] most of the reports in the literature have dealt with the effects of deficient diets in animals or human beings when the lack of vitamin B was likely to be great. Reporting on 125 babies from a nursery in an obstetric ward, Hoobler [19] stated: "About 1 out of 6 of the infants studied showed symptoms of rigidity." This indicates that the diets of the mothers had lacked vitamin B during their pregnancy, since he went on to say: "This symptom disappeared in all but 6 cases, indicating that the quantity of vitamin B needed by infants differs greatly." The result of

14. Maurer, S., and Tsai, L. S.: The Effect of Partial Depletion of Vitamin B Complex upon Learning Ability in Rats, J. Nutrition **4**:507, 1931.

15. Bernhardt, K. S.: The Effect of Vitamin B Deficiency During Nursing on Subsequent Learning in the Rat, J. Comp. Psychol. **17**:123, 1934.

16. Anderson, J. E., and Smith, A. H.: The Effect of Quantitative and Qualitative Stunting upon Maze Learning in the White Rat, J. Comp. Psychol. **6**:337, 1926.

17. Balken, E. R., and Maurer, S.: Variations of Psychological Measurements Associated with Increased Vitamin B Complex Feeding in Young Children, J. Exper. Psychol. **17**:85, 1934.

18. Hoefer, C., and Hardy, M. C.: Later Development of Breast Fed and Artificially Fed Infants: Comparison of Physical and Mental Growth, J. A. M. A. **92**:615 (Feb. 23) 1929.

19. Hoobler, B. R.: Use of Vitamin B in Diets of Infants, J. A. M. A. **96**:675 (Feb. 28) 1931.

increasing the vitamin content of the food has largely been measured in terms of stimulated growth, particularly as it applies to weight. In other studies, in which the diets might have been considered more nearly adequate, the subjects were described by the authors as undernourished and considerably under par. With the groups of children observed by Summerfeldt [12] and Ross and Summerfeldt [13] there is the complicating fact that they were in an institution and although regarded as normal were probably not exactly comparable to children living in their homes under the care of their own parents.

Thus, it is clear from a review of the literature that the evidence presented in relation to the addition of vitamin B to the diet in early life has to do largely with the effect of adding vitamin B to the food of infants or young animals when the diet was known to be deficient and with the effect on undernourished children or on children confined in institutions.

The latest and most complete study was recently reported by Elias and Turner.[20] They observed a group of 238 well infants living in homes in the neighborhood of the Bellevue Hospital. These babies were observed at frequent intervals from the third week to the end of the first year of life. One hundred and twenty-one received vitamin B complex in their daily food in the form of wheat germ and brewer's yeast, while 117 did not get this supplement and were used as controls. From the observations made, the authors concluded that "supplementing the diet of artificially fed infants with additional vitamin B did not exert a favorable influence on the rate of growth, the incidence of upper respiratory infections and the incidence of gastro-intestinal disturbances during the first year of life."

There does not appear to be much conflict of opinion about the effect of deficiency of vitamin B and the consequent beneficial action of supplementary vitamin B. Our study was undertaken because of the contradictory evidence as to the value of adding supplementary vitamin B to the usual diet of healthy infants. The purpose of the study was to determine whether or not the early addition of the antineuritic factor, vitamin B_1, in the form of a water extract of rice polishings to an ordinary milk formula represented a nutritive advantage to the health of the average artificially fed healthy infant during the first twelve months of life. The program was made sufficiently broad by the utilization of many of the measurements and methods developed in recent research in child development, so that, in addition to the increase in stature and in weight, which are the usual criteria of good health in infancy and in childhood, we might be able to measure some of the

20. Elias, H. L., and Turner, R.: A Clinical Study of the Influence of Vitamin B Supplements, J. Pediat. **8**:352, 1936.

less readily detectable changes. In other words, we endeavored to measure growth in numerous directions, or to note change in the infant's "plane of health."

SUBJECTS AND METHODS OF STUDY

The methods are described in detail in this report, since it serves as a basis for a group of studies on growth. The subjects were 193 normal, full term infants[21] living in their own homes and cared for by their own parents. The babies observed during the year 1934-1935 were entirely artificially fed after the first visit, but in 1933-1934 a few babies were partly breast fed. The babies ranged in age from 5 days to 2½ months at the time of the initial observation. The average age was 5½ weeks at the beginning of the study and approximately 12 months at the conclusion. A number of the infants studied returned for examination and measurement at the age of 2 years.

The nurses delivered supplies, made regular visits to the homes, instructed the mothers in the management of the infants and assisted in the clinic in taking the anthropometric measurements and the roentgenograms, in taking and filing the records and in giving general instructions to the parents.

The physical measurements and the medical examinations of the 193 infants were made by the same two pediatricians (M. W. P. and B. M. H.) throughout the study. Appointments were made once a month for the visit to the clinic. At these visits, information was obtained regarding feeding management, home care, health and nutritional and developmental progress. Instructions were then given for the care and management of the infants during the intervening period, to the time of the next appointment.

A diligent attempt was made to accept for study only average well babies. We attempted to approximate a cross-section of the indigent and near-indigent class of the cosmopolitan population of Detroit. Approximately two thirds of the infants selected were white, and approximately one third, Negro. It was felt that a carefully controlled study through a clinic, under close medical and nursing supervision, with the infants living in the natural environment of their own homes, would give as dependable information on the average expectancy in nutrition, growth and development from the quantitative consumption of specific food factors as would a similar study conducted with infants living under the conditions existent in the usual hospital or boarding home.

As a part of the initial record for each patient, any information relative to the prenatal and natal factors which might possibly influence the nutrition, growth and development of the infant was obtained. Details were secured concerning the mother's diet and health during and following pregnancy. The body type of the parents, their racial extraction and education and the conditions in the home were recorded. A history was obtained relative to the prior management and health of the infant. All these factors are important in the interpretation of the nutritional development of the child. If a congenital or inherent abnormality was detected at the time of the initial examination or subsequently, the infant was rejected from the study. Twins and infants born prematurely were not accepted for study because of their predisposition to subnormal nutritional development during the first year of life.

21. The infants were obtained through the cooperation of the Detroit Department of Health, the Harper Hospital, the Florence Crittenton Hospital, the Woman's Hospital and private physicians in Detroit.

At the first visit to the clinic, the babies were assigned each year alternately to two groups. Group I-B and group II-B received a routine formula containing evaporated milk to which at the time of manufacture had been added vitamin B (B_1) in the form of a water-soluble extract of rice polishings.[22] The control group, group II, received the same routine formula, but the evaporated milk contained no vitamin B extract. Group I-B was observed during the year 1933-1934, while groups II and II-B were observed during 1934-1935.

The diet of the infants was controlled as rigidly as possible under the circumstances. The basic, or control, formula for all the infants under observation included evaporated milk, water and corn syrup, the mixture being acidified by the addition of commercial dehydrated lemon juice powder,[23] which was used in a standard amount sufficient to supply the antiscorbutic requirements. Table 1 shows the variations in the formulas for the different groups of infants studied.

Cereal (milled, with a low vitamin content) feedings were added to the diets of all the infants at the age of 4 or 5 months, strained carrots and peas (potatoes, if the child had a large appetite and desired them in addition to the other vegetables) at 5 or 6 months, prune pulp and apple sauce at 6 or 7 months and eggs at 11 months. These ages were selected for the addition of the supplemental foods because they represented average pediatric practice.

The variations in diet included the addition of vitamin B and the use of irradiated and nonirradiated evaporated milk. When cod liver oil was used as the antirachitic source, it was given in quantities containing from 250 to 600 U. S. P. units of vitamin D per day.[24]

During 1934-1935 both groups of babies received a larger intake of milk and an increased amount of vitamin D in the form of cod liver oil. In this year, 66 infants received the evaporated milk fortified with vitamin B (group II-B), and 51 control infants (group II) had the basic formula without increased vitamin B.

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22. All the milk was collected in the same community and prepared under identical conditions in one evaporating plant. Although the water extract of rice polishings was added to one batch, the milk was similar to commercial evaporated milk as to physical appearance, consistency, taste and chemical analyses. Mr. G. C Supplee, Ph.D., of the Research Laboratories of the Dry Milk Company, Inc., made the biologic tests. The evaporated milk fortified with a water extract of rice polishings and the unfortified milk were shown to contain from 2 to 2.7 and from 0.7 to 1 Sherman-Chase units of vitamin B per gram of solids, respectively. Assays demonstrated also that the vitamin D content of the fortified irradiated evaporated milk when reconstructed contained an equivalent of from 160 to 175 U. S. P. units of vitamin D per quart (946 cc.) (1:1).

23. The dehydrated lemon juice powder showed by titration (Bessey, O. A., and King, C. G.: The Distribution of Vitamin C in Plant and Animal Tissues and Its Determination, J. Biol. Chem. **103**:687, 1933) from 0.803 to 0.879 mg. of vitamin C per gram and contained 13 Sherman-Chase units of vitamin B per gram. The nutritive value of this product in infant feeding is to be reported in the near future. Givens, M. H., and McClugage, H. B.: The Antiscorbutic Property of Fruits: I. An Experimental Study of Dried Orange Juice, Am. J. Dis. Child. **18**:30 (July) 1919. Givens, M. H., and Macy, I. G.: The Antiscorbutic Property of Some Desiccated Fruit Juices, J. Biol. Chem. **46**:xi, 1921.

24. One batch of standardized cod liver oil specially preserved and held in cold storage was used throughout the study.

The average estimated vitamin B_1 content of the supplemented formula was approximately 320 Sherman-Chase units. The effect on the infants of augmented intake of vitamin B in the form of an aqueous extract of rice polishings in a diet otherwise known to contain all the nutritive essentials can be more clearly demonstrated by the 1934-1935 group of babies, because in these infants the possible complicating factor of inadequate amounts of vitamin D was eliminated by the inclusion of cod liver oil. An attempt was made to increase the consumption of milk after the age of 8 weeks by using somewhat less water in the formula and by planning to have the day's formula contain one can of evaporated milk (approximately 13½ ounces [399 cc.] by volume) by the time the infant reached the age of 4 months. For uniformity, this level of milk consumption was maintained thereafter. The only difference between the diets of the infants in group II

TABLE 1.—*Variations in the Formulas Used*

	No. of Infants Studied		Approximate Daily Vitamin Content of Formulas	Average Daily Consumption of Reconstructed Milk (1:1)	
	Accepted	Observed Over 2 Months		Ounces	Cc.
Group I-B (with supplementary vitamin B; 1933-1934)	89	76	Rice polishings-supplemented formula—320 Sherman-Chase units of vitamin B; milk irradiated—95-135 U. S. P. units of vitamin D; formula contained approximately 14 mg. of vitamin C (4 tsp. of lemon juice powder added)	22.2	657
Group II (without supplementary vitamin B; 1934-1935)	56	51	Evaporated milk formula—227 Sherman-Chase units of vitamin B; cod liver oil—250-600 U. S. P. units of vitamin D; formula contained approximately 14 mg. of vitamin C (4 tsp. of lemon juice powder added)	22.7	672
Group II-B (with supplementary vitamin B; 1934-1935)	74	66	Rice polishings-supplemented formula—320 Sherman-Chase units of vitamin B; cod liver oil—250-600 U. S. P. units of vitamin D; formula contained approximately 14 mg. of vitamin C (4 tsp. of lemon juice powder added)	23.3	689
Total number of infants studied.....	219	193			

and II-B was in the amount of vitamin B given, since the formula was supplemented at the same time with like amounts of cereal, vegetables and fruits, as before described.

Seventeen anthropometric measurements [25] were made at the initial visit and at each subsequent visit. Girths were measured by the metric tape with a constant tension Gülick spring handle; biacromial width and tibial length, with the small caliper; the measurements of the head and chest and intercristal width, with the anthropometer, and recumbent, stem and leg lengths, on the measuring board (fig. 1).

Each infant was seen in the clinic two weeks after the initial examination in order that we might make sure that the mother and baby had become established in the suggested routine. Subsequent examinations were made at

25. The anthropometer and calipers were made and standardized in the laboratory of the Brush Foundation, Cleveland, through the cooperation of Dr. T. Wingate Todd.

approximately four week intervals until the baby had reached 1 year of age. During 1934-1935 1,350 visits were made to the clinic, many of the infants coming in for from 11 to 12 visits each.

The mothers were questioned at each visit regarding their babies' appetite, digestion, vomiting, bowel movements, eruption of teeth, sweating of the head, sleep, behavior, illness and length of exposure to sun and fresh air. The questioning was greatly aided by the mother's bringing with her a daily record of the amount of food consumed, the number of bowel movements, the amount of water taken and the number of times that the baby regurgitated or vomited. Special attention was given to the procedure of making the formula, the mechanics of feeding and the administration of the supplementary foods. After the anthropometric measurements were made, the babies were examined for evidence of rickets or other abnormalities.

On the basis of the reports submitted by the mothers and the nurses' reports on the homes and the mothers' care in the homes, it appears that in spite of the fact that most of the families represented were of the indigent or near-indigent class, the parents of our babies were of a fairly high caliber and took satisfactory care of the infants. This probably accounts for the excellent cooperation of

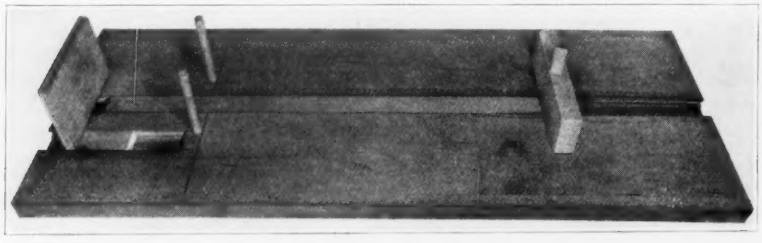

Fig. 1.—The measuring board.

the parents through the whole period of study. The degree of cooperation was more striking because the clinic was situated at a considerable distance from the bus and car lines and the babies were brought in even in the severest weather.

As the blood picture is an integral part of the child's physical status, studies of the blood were made on the initial visit and at four week intervals thereafter. Total white counts were made only when indications demanded, but estimations of the hemoglobin by the Haden-Hausser hemoglobinometer were made, red cell counts were done and smears for differential leukocyte counts were taken at each visit. Fresh specimens of urine were secured from each subject during the first year of the study and the usual qualitative tests made. This practice was discontinued during the second year because it did not seem to yield any information bearing on the problems. In order that the probable personal error might be reduced, only three laboratory technicians were employed during the two year period to do the work connected with the studies of the urine and the blood. All samples of blood for the counts and the estimations of hemoglobin were taken at about the same time of day, between 10:30 a. m. and 12:30 p. m. Notations were made as to whether the child was asleep, crying, quiet or restless and as to the time of the last feeding.

Monthly roentgenograms were made, a technic which gave the maximum detail at a minimum exposure time being used. The details of this procedure will be described in a subsequent paper. Four exposures were taken each time. With the infant in a supine position, an anterior-posterior view of the arm, including

the elbow and the wrist, a posterior-anterior view of the hand, including the wrist, and an anterior-posterior view of the foot were made. With the baby in a prone position, a fourth exposure was made, of the posterior-anterior view of the leg, including the knee and the ankle.

These films enabled us to measure the growth of the bones, as exemplified by that of the tibia, and to check evidence of rickets, scurvy and any other abnormalities and the degree of mineralization of the bones.[26]

Quantitative measurements were made of the extent of ossification and of the linear dimensions and areas of various bones. The tibia was selected for measurement because it is apparently representative of the development of the skeletal and body type. The landmarks adopted were those selected by Bakwin and Bakwin[27] for measuring diameters and lengths on the tibia. The equipment necessary for determining these lengths and areas is a working surface illuminated

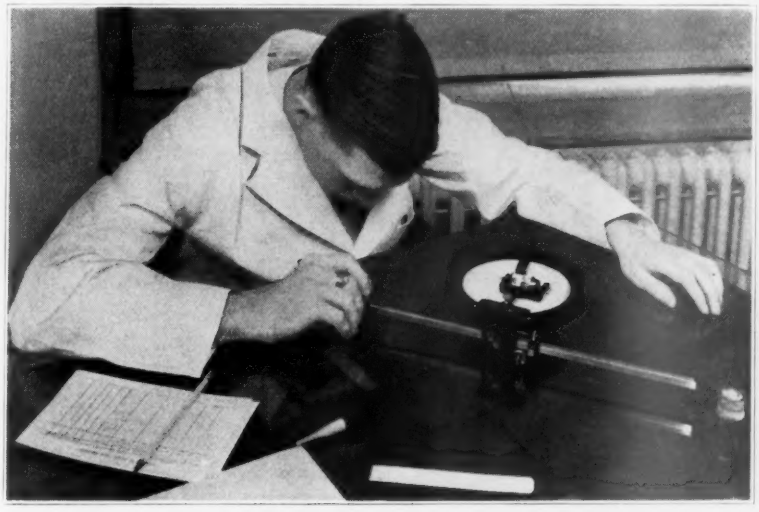

Fig. 2.—Measuring the bones with the planimeter.

from below, a scale for linear measurements and a planimeter. The precision disk planimeter[28] chosen was one that had been found the most accurate for work of this nature by Baldwin and his associates.[29]

26. Lawrence Reynolds, M.D., roentgenologist, cooperated in reading and interpreting all the roentgenograms.

27. Bakwin, H., and Bakwin, R. M.: External Dimensions of the New-Born, Am. J. Dis. Child. **48**:1234 (Dec.) 1934; Body Build in Infants: VIII. Influence of Retarded Growth on the Dimensions of the Ulna and the Radius, ibid. **49**:876 (April) 1935.

28. The precision disk planimeter was manufactured by G. Goradi at Zurich, Switzerland.

29. Baldwin, B. T.; Busby, L. M., and Garside, H. V.: Anatomic Growth of Children: A Study of Some Bones of the Hand, Wrist and Lower Forearm by Means of Roentgenograms, Studies in Child Welfare, Iowa City, University of Iowa, 1928, vol. 4, no. 1.

The length of the tibia was measured from the proximal to the distal margin of the shaft parallel to a median line. As the epiphyses are not ossified in infants, only the shaft proper was considered. The diameter of the distal metaphysis was measured perpendicular to the median line, as was the diameter of the shaft. The latter was measured at a point one third of the total length of the shaft from the distal margin [27] (figs. 2 and 3).

To determine area, the outline of the bone was traced three times. This gave three values, one of which represents a single tracing; one, the mean of two tracings, and the third, the mean of the three tracings. The median (or modal) figure was assumed to be the true area if it did not differ from at least one of

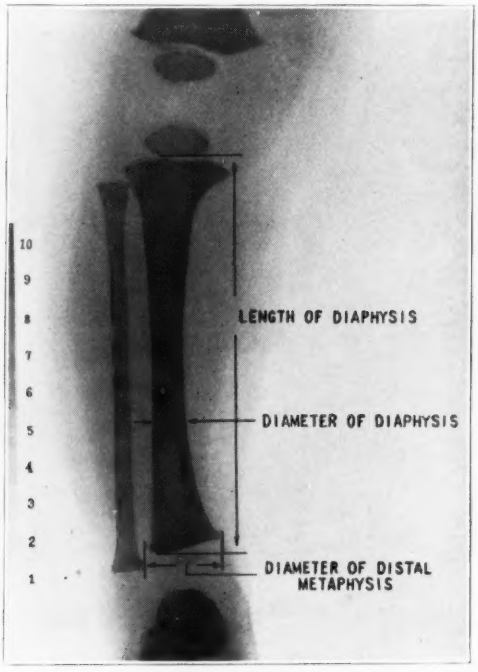

Fig. 3.—Roentgenogram of a left tibia.

the other figures by more than 5 sq. mm. This amount represented a variation of less than 1 per cent for even the smallest tibias. Usually the variation was not so great. In cases in which the variations between readings was greater than 5 sq. mm., the whole measurement was repeated.

Since no studies were available on the use of dehydrated lemon juice powder as an antiscorbutic agent in the feeding of infants, the roentgenograms were carefully studied for any indications [26] of the changes in the bones described as preclinical scurvy by Park and his co-workers.[30] As an added precaution during the first year, the babies were given a capillary resistance test at or near the age

30. Park, E. A.; Guild, H. G.; Jackson, D., and Bond, M.: The Recognition of Scurvy with Especial Reference to the Early X-Ray Changes, Arch. Dis Childhood **10**:265 1935.

of 6 months to determine whether or not there was evidence of increased capillary permeability. The method used was that of Göthlin.[31] Only 1 infant was found to have more than 7 petechiae. His condition was diagnosed as clinical scurvy. No lemon powder had been given by the mother throughout the whole period of observation. It has been stated that the capillary strength ascertained in this way reveals indirectly the vitamin C standard of healthy infants and aids in the diagnosis of latent scurvy. Göthlin expressed the opinion that the vitamin C intake of a healthy person is normal when there are less than 5 petechial spots and subnormal when there are over 8.

During the first year of observation (1933-1934) the computation of the average consumption of milk in group I-B was complicated by a continuation of breast feeding by some of the mothers and by comparative inefficiency in keeping satisfactory records. In this group the intake of both vitamin B and vitamin D was reduced in any instance in which partial breast feeding was being used because of the smaller amount of the formula consumed.

After the growth clinic became better known, during the second year (1934-1935), and its reputation became better established in the community, it was possible to eliminate all breast-fed babies from groups II and II-B after the first visit or two. In a like manner, only the mothers who were more successful and reliable in keeping reports on food intake were retained. In compiling the data on the food intake for the infants of group I-B it was necessary in some cases to base them on prescribed amounts and probable consumption, when actual records were not available. Because of these facts, the records for groups II and II-B are more reliable and satisfactory than those for group I-B.

The gross average daily consumption of reconstructed evaporated milk (diluted 1:1) of the babies from 28 to 392 days of age was 22.2, 22.7 and 23.3 ounces (657, 672 and 689 cc.) for group I-B, group II and group II-B, respectively (table 1).

RESULTS AND COMMENT

Figure 4 shows the relationship between the average intake of milk fortified with vitamin B and the average growth in weight and height. During the first two hundred days the milk intake was superior in group II-B, while the average weights of the infants of group II-B remained superior to those of the babies in group I-B throughout the entire period. The average heights of the two groups showed little difference, those of II-B being marginally superior.

In evaluating the persistent superiority shown in the weight curve of group II-B, one must consider several possible reasons: (1) a greater intake of milk and calories, (2) a larger intake of vitamin B as a result of greater consumption of milk, (3) stimulation of the appetite due to the vitamin B and a resultant consistently greater intake of food, (4) better utilization of food brought about by a more liberal intake of vitamin B and (5) a more adequate allowance of vitamin D.

31. Göthlin, C. F.: Methode zur Bestimmung der Festigkeit der Hautcapillaren und zu indirekter Beurteilung des individuellen C-Vitamin-Standards, Klin. Wchnschr. **11**:1469, 1932.

For the infants of group I-B the consumption of vitamin D was from 95 to 135 U. S. P. units in the form of irradiated milk, and for group II-B the intake was from 250 to 600 U. S. P. units in the form of cod liver oil.

The comparison of the efficiency in the utilization of milk by the infants receiving supplementary vitamin B (group II-B) and that of the infants without vitamin B (group II) is shown in figure 4. The degree of efficiency was calculated by dividing the average daily gain, in 10 Gm. units, by the number of ounces (28.35 Gm.) of reconstructed milk (1 : 1) consumed. The figures for food consumption represent only the consumption of infants who received the milk formula as the sole

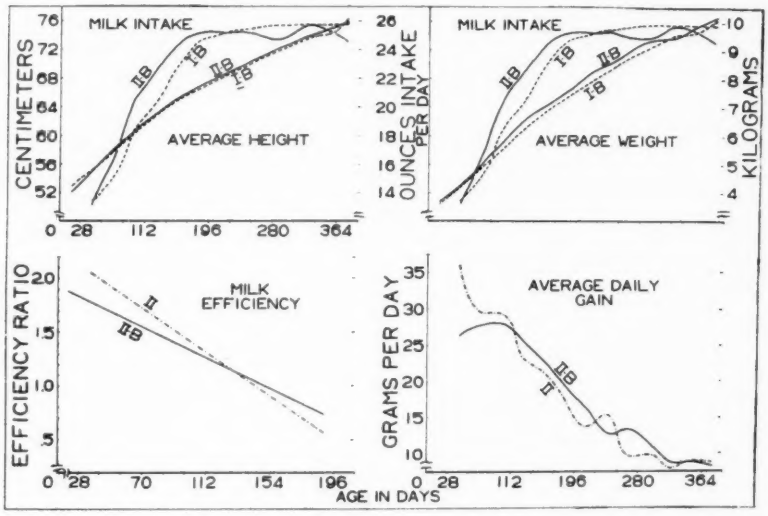

Fig. 4.—Graphs showing the food utilization.

food after breast feeding had been discontinued and before supplements of solid foods had been introduced. It may be noted that group II-B at first showed a lower utilization than the control group (group II). However, after about the one hundred and twenty-sixth day the utilization of the group receiving fortified milk became superior.

Figure 4 illustrates the average daily gain in weight of the infants during 1934-1935, when the food taken differed only in the vitamin B content and so was free from the other variables mentioned above. In general, the group receiving the supplement of the extract of rice polishings (group II-B) gained weight more consistently and with less variation than the group without this added nutrient. The fact that the more rapid average daily gain of group II-B occurred at approximately the time when the degree of utilization of the food

became superior and surpassed that of the control group, group II, may be of significance (fig. 4). What we believe are the reasons for the difference in the rate of growth for the two groups and the more regular and stable curve for the infants receiving the vitamin B supplement will be amplified in our consideration of the other curves. We believe that vitamin B has a stabilizing effect on growth and nutrition.

An accelerated gain in weight has been identified as one criterion of the optimal vitamin B intake for growing animals,[4] infants [32] and children.[33] Figure 4 illustrates the average growth in weight of the control infants (group II), who received no additional vitamin B, and the experimental babies (group II-B), who received supplementary vitamin B. It may be noted that an increase of from 30 to 50 per cent in the vitamin B intake did not produce a significant difference in the average rates of growth in weight of these two groups of healthy babies. The average estimated vitamin B content of the nonsupplemented formula was *227* Sherman-Chase units. Both groups of babies, whether they had additional vitamin B or not, grew faster than those represented in the standard growth curve of the United States Children's Bureau [34] and as well or better than the superior group of infants studied by Stuart [35] in Boston (fig. 5). Perhaps an explanation of our negative results lies in the probability that the basic dietary formula of these babies during 1934-1935 contained sufficient nutrients to satisfy the maximum impulse of growth, so that a further increase in the vitamin B level of the diet could not further stimulate the processes of growth.[4] This failure to produce an increase in the average weight of a group of infants with vitamin B is in accord with the finding of Elias and Turner,[20] who observed a similar group of normal infants, and is in contrast to the results of other studies previously discussed. We wish to point out the fact previously alluded to that while the growth curves of groups II and II-B are similar, there is considerable difference between these and the curves for group I-B for reasons other than the augmented vitamin B given to group I-B. This illustrates clearly the necessity of maintaining all the other dietary essentials and accessory factors at an optimal level before placing any interpreta-

32. Bloxsom, A. P.: Vitamin B Requirements in Infancy, Am. J. Dis. Child. **37**:1161 (June) 1929. Hoobler.[2] Dennett.[5] Bartlett.[6] Gaynor and Dennett.[7]

33. Knott, Elizabeth M.: A Quantitative Study of the Utilization and Retention of Vitamin B by Young Children, J. Nutrition **12**:596, 1936. Morgan and Barry.[11] Summerfeldt.[12] Ross and Summerfeldt.[13]

34. Woodbury, R. M.: Weight-Height-Age Tables for Boys and Girls from Birth to School Age, United States Department of Labor, Children's Bureau, 1923.

35. Stuart, H. C.: Standards of Physical Development for Reference in Clinical Appraisement, J. Pediat. **5**:194, 1934.

tion on the effects of an increase in the vitamin B content of a diet, and it may help to account for some of the conflicting opinions as to the results of such an increase.

The infants of group I-B had an average of 1.1 ounces (31 Gm.) less of reconstructed milk in their daily rations than the other babies who received supplementary vitamin B (group II-B). While this small superiority of milk intake may have been a factor, a more adequate intake of vitamin D probably played a larger part in the superior nutritional state of the babies during 1934-1935. Its effect was shown in both height and weight. These findings are in accord with the

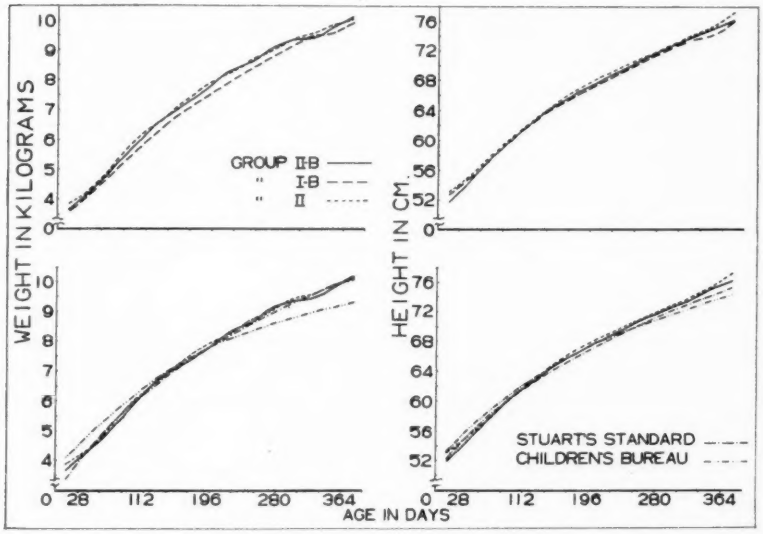

Fig. 5.—Graphs showing the group averages for weight and height.

recent demonstration of Stearns, Jeans and Vandecar [36] that the growth in the length of infants given 1 teaspoonful of high grade cod liver oil (from 340 to 400 U. S. P. units of vitamin D) daily is superior to the rate of linear growth of infants receiving the same type of diet but with irradiated milk as the source of vitamin D (from 60 to 135 U. S. P. units of vitamin D daily).

Although Hoobler's study [19] over a five month period indicated that a supplement of vitamin B resulted in a greater growth in recumbent and stem lengths, our results do not corroborate his findings. In fact, if there was any advantage it was in favor of the control group,

36. Stearns, G.; Jeans, P. C., and Vandecar, V.: The Effect of Vitamin D in Linear Growth in Infancy, J. Pediat. **9**:1, 1936.

group II, without the vitamin B supplement (fig. 6). Such lack of agreement emphasizes the necessity of continuing observations on infant growth for prolonged periods, since some of our measurements showed a superiority in one or another group which was not maintained for a considerable time.

Part of the total length, or height, is made up by the long bones of the leg. Of these the tibia is the easiest to measure because the bony landmarks are readily seen, close to the skin, and anthropometric measurements can be quickly and accurately made. Figure 6 shows the average tibial length as measured by the small caliper. The curves are considerably different for the two groups (II and II-B), owing

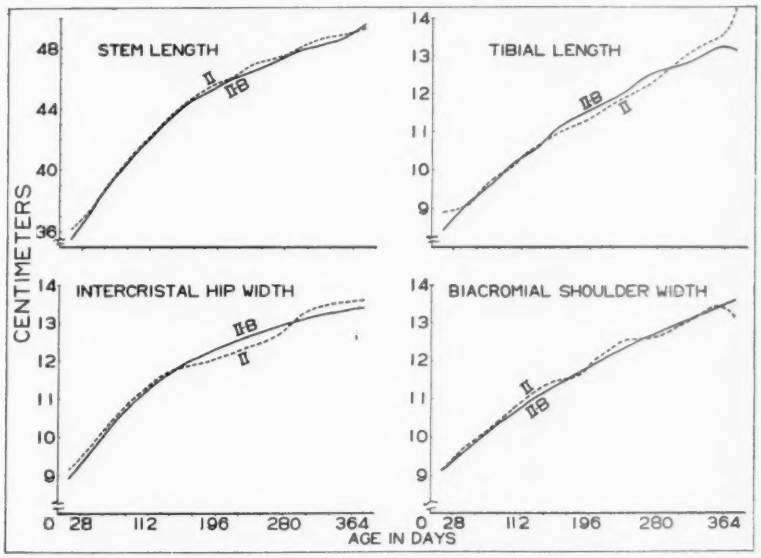

Fig. 6.—Graphs showing the average anthropometric measurements.

chiefly to the depression of the curve for group II (without a supplement of vitamin B) when the infants were from approximately 140 to 290 days old, which depression is followed by a rise above the level for group II-B, who received additional quantities of this factor.

The curves for tibial length in figure 6 are similar to the curves for the average intercristal (hip) width for the same two groups of babies. Intercristal width and tibial length are two of the more accurate anthropometric measurements, so the technical error should be small. The exact interpretation of the lag in the growth of the bones of the pelvic girdle and of the tibia from about the one hundred and fortieth to the three hundredth day is difficult. The beginning of the period corresponds fairly closely to the time when the efficiency in the utiliza-

tion of milk became greater (fig. 6) in the infants receiving the vitamin B supplement. These curves illustrate clearly the more constant and regular progression of growth in these two types of bones, which we have termed stabilization. Further analysis of our data and of other investigations may shed some light on the reason for this difference in the metabolic processes during this particular period.

The corresponding graphs (fig. 6) for biacromial (shoulder) width show little divergence at any point, although the group receiving no additional vitamin B (group II) showed a more irregular increase in shoulder width. In contrast to the intercristal (hip) width, which is

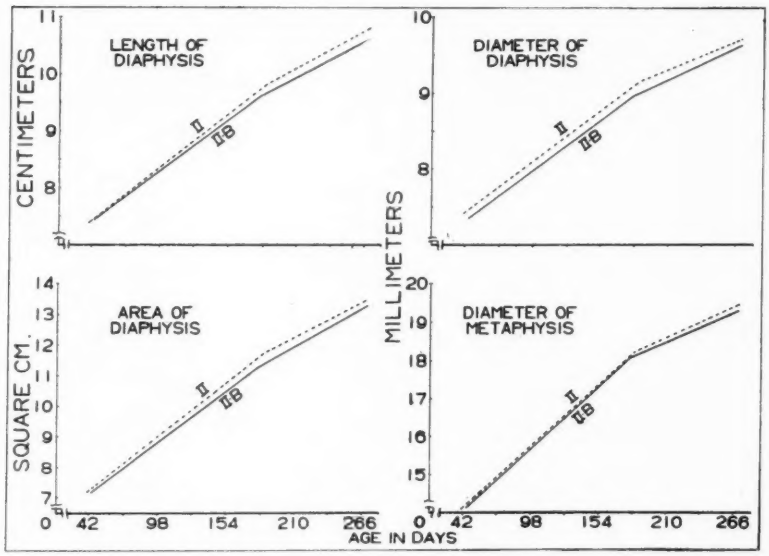

Fig. 7.—Graphs showing the average dimensions of the left tibias as taken from roentgenograms.

reliable in measurement and consequently for interpretation, the biacromial diameter is much less accurate as a measure of growth because it can so readily be changed by voluntary muscular effort on the part of the child.

Measurements were also made of the different parts of the tibia from roentgenograms taken on admission and at approximately the sixth and the ninth month (figs. 2 and 3). Figure 7 shows the average lengths of the tibial diaphysis to be little different except at the ninth month, when those of the infants of group II were much superior. If these curves are further analyzed, according to the influence of sex on the bony structure, the girls in group II-B are seen to have had shorter diaphyses than the boys and to have depressed the mean value for the

entire group. The diameters of the diaphysis of the left tibia as well as the areas exhibited wide differences according to sex but only slight differences according to group (fig. 7). The average diameters of the distal metaphysis showed similar differences according to sex and almost negligible differences according to group.

We turned next to a study of the measurements of the various circumferences of the body in an effort to determine the relative effectiveness of augmented intakes of vitamin B. Figure 8 illustrates the average circumference of the thigh in the two groups (II and II-B). While there is little difference in the curves at any point, the curve

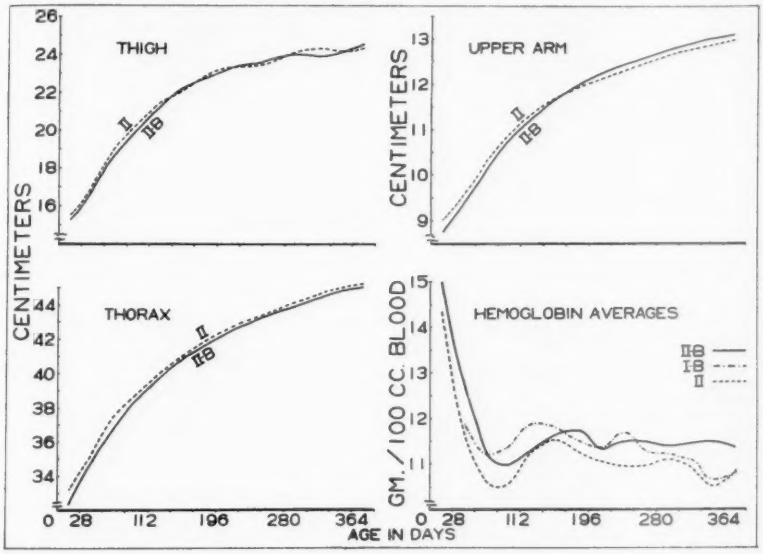

Fig. 8.—Graphs showing the average anthropometric circumferences and hemoglobin levels.

representing the babies who did not get the vitamin B supplement is more irregular. This again illustrates the stabilizing effect of an augmented vitamin B intake, this time in the state of the soft tissues rather than in the growth of the bones. In infancy the thigh is an important depot for fat storage, so that any alteration in the nutritional state is rapidly shown in this region.

The two groups showed small differences in the average circumference of the left arm, the average for group II following that of II-B after about the one hundred and fiftieth day and remaining lower from that point on (fig. 8).

The circumference of the chest differs from that of the thigh or the arm in that its largest component part is the bony framework

of the thorax while the smallest is the overlying soft tissues. This measurement also is open to error, because of the movement of respiration. Figure 8 shows that the infants of group II (without vitamin B supplement) had a slightly greater average circumference of the chest throughout.

The other anthropometric measurements, which have not been considered in detail, have not been worked out as yet in the form of a chart or table. A more detailed analysis of the data on these measurements may reveal significant differences in the growth of individual babies that are now masked by group averages.

Dentition.—Because dentition is often considered in relation to skeletal development, the time of appearance of the deciduous teeth for the infants in group II-B, who received additional vitamin B,

TABLE 2.—*Average Number of Teeth per Infant at Various Ages*

Age Interval, Days	Group II-B			Group II		
	Total Teeth	Total Infants	Average No. of Teeth per Infant	Total Teeth	Total Infants	Average No. of Teeth per Infant
112-140	3	65	0.04	4	46	0.08
141-168	6	53	0.11	14	47	0.29
169-196	29	61	0.47	27	44	0.38
197-224	49	51	0.96	50	45	1.11
225-252	112	57	1.96	72	42	1.71
253-280	150	54	2.77	114	41	2.78
281-308	158	41	3.85	159	36	4.41
309-336	200	50	4.40	158	32	4.93
337-364	222	42	5.23	195	31	6.29
365-392	100	15	6.66	41	7	5.85
Age in days at appearance of first tooth:						
Number of infants.		59			43	
Age range, days....		131-340			101-340	
Mean age, days....		221.26			226.43	

was compared with that for the infants in group II, who did not receive this dietary supplement, and little difference was observed, as indicated in table 2.

Physical and Metabolic Disturbances That Affect the "Plane of Health."—As an infant's ability to resist bacterial invasion of the body is assumed to be one of the indexes of buoyant health, we kept a record of the number of infections suffered by each baby. Table 3 illustrates the occurrence of each type of infection and the severity of each attack of infection, diarrhea or eczema for each group and the average number of attacks suffered by each infant.

It may be noted that when all grades of severity of nasopharyngitis (common cold) were added to bronchitis and pneumonia the number expressing "infections per infant" was 3.23 for group II, 3.9 for group I-B and 4 for group II-B. There were practically the same number of aural complications in groups II, I-B and II-B.

Diarrhea was practically always of the parenteral type associated with an infection of the respiratory tract. None of the infants had diarrhea severe enough to make hospitalization or the parenteral administration of fluids necessary. In most of them the condition cleared up within a few days, simply because the food intake was reduced and the initial infection cleared up. There were more cases of mild diarrhea in groups I-B and II-B than in the group who did not receive the vitamin B supplement (group II). While it is true that the increased frequency of the bowel movements was initiated by or coincident with infection and can therefore properly be classified as parenteral, the vitamin B contained in the aqueous extract of rice polishings apparently exerted a mild laxative effect. The condition being mild, the diarrhea responded readily to treatment, so that, on the whole, the greater number of cases in the groups given supplementary vitamin B was relatively unimportant.

TABLE 3.—*Occurrence of Infections, Diarrhea and Eczema*

	Group II		Group I-B		Group II-B	
	Total	Per Infant	Total	Per Infant	Total	Per Infant
Number of babies	51		76		66	
Nasopharyngitis						
Moderate or severe	40	0.78	80	1.08	64	0.97
Mild	120	2.35	203	2.74	128	2.94
Otitis media	9	0.18	12	0.16	8	0.12
Bronchitis and pneumonia	5	0.10	13	0.17	12	0.18
Diarrhea	11	0.22	38	0.51	22	0.33
Specific diseases	8	0.16	17	0.23	20	0.30
Eczema	6	0.12	10	0.13	13	0.20

Persistent constipation was a symptom rarely observed in any group of infants. It was noted six times in group II-B and seven times in the control group (group II). In these babies the constipation lasted so long that alteration in the diet or other treatment was required. The infants who suffered for only a day or two, during or after an illness or other upset, were not considered as having constipation. It appears that the diets of the infants in group II did not tend to produce constipation except in a small number of babies.

Severe vomiting which continued for more than a day or two was encountered twice in group II-B, each time accompanying an infection of the respiratory tract. There were two attacks in the control infants, one appearing with an infection of the respiratory tract and the other without apparent cause.

Because of the uniformity with which anorexia is found in experimental animals when their diets are deficient in vitamin B and the striking improvement that occurs after this substance is added to such deficient diets,[8] the refusal of food has been regarded as one of

the prime indications of a lack of vitamin B in human beings. Therefore, it seems logical to assume that if the vitamin B content of the diet in the control group of infants was below the optimal amount more infants should have suffered from anorexia in this group than in the group who were given from 90 to 100 additional units of vitamin B_1 (Sherman-Chase) per day. In reviewing the records of our infants, we found that there were 8 babies whose mothers complained of their refusal of food for more than a few days among those who did not receive the vitamin B addition while there were 10 among the infants in group II-B. When expressed in percentage the number of cases of anorexia was approximately equal in each group.

Rejection of food during illness is an almost constant finding for babies and is not to be regarded as true anorexia in the sense that the term is generally understood. It is of course conceivable that a dietary deficiency, particularly of vitamin B, might cause the transient periods in which food is refused to be more numerous or more prolonged. With this in mind, we recorded the number of occasions during which infection caused a baby to stop eating for a short period. There were twenty-six (39 per cent) such episodes in group II-B and nineteen (37 per cent) in the group who did not receive the vitamin B supplement.

There were few instances of eczema in either the control group or the group who had additional vitamin B. The slight difference between the three groups is probably not of significance.

Detailed psychometric measurements were made on a number of these babies, but the results will be reported in a separate paper by Dr. Martha G. Colby, of the University of Michigan.[37] We did, however, record the ages at which the accomplishments were first noted that are ordinarily taken as measures of the degree of development of the nervous system. The most reliable of these are probably the infant's ability to sit without support, to crawl, to speak words and to walk alone. The differences in the mean ages at which these abilities were first observed were slight in all the groups. For instance, the ability to speak words was noted at the mean age of 270 days in the control group (group II), at 274 days in group I-B and at 276 days in group II-B.

Although the infants were given vitamin D in the form of either irradiated milk or standardized cod liver oil, they were not 100 per cent protected against rickets, as is usually found in clinical experience. Dehydrated lemon juice powder furnished the supplemental antiscorbutic agent in quantities in keeping with average pediatric practice. In the infants of group II-B there was no instance of clinical scurvy. From

37. Colby, Martha G.; Macy, Icie G.; Poole, Marsh W.; Hamil, Brenton M., and Cooley, Thomas B.: Relation of Increased Vitamin B (B_1) Intake to Mental and Physical Growth of Infants: Preliminary Report, Am. J. Dis. Child., this issue, p. 750.

examination of the roentgenograms [26] 1 infant was classified as having slight evidence of preclinical scurvy. In another infant the condition was diagnosed as moderately severe scurvy with severe rickets. In 3 babies moderately severe rickets developed at some time during the year, as evidenced by roentgen examination. In the control group, group II, there were 3 roentgen diagnoses of moderate rickets and only 1 of severe rickets. Three babies were classified as having mild or very mild scurvy, none of whom presented any evidence of scurvy on physical examination.

Hematologic Studies.—A study of the hemoglobin values and the cellular elements of the blood was made a part of the monthly observation of the infants as an aid in evaluating their nutritional state. The data reported here pertain to hemoglobin values only.

The curves representing average hemoglobin levels for the two groups given supplementary vitamin B (II-B and I-B) and the control group (group II) are shown in figure 8. The curve for group II-B is more regular in contour than the others after the initial drop in the first few weeks. It is also a little higher during the latter portion of the observation period.

CONCLUSION AND COMMENT

The average daily gain in weight of the infants receiving supplementary vitamin B during the year 1934-1935 (group II-B) was found to be more regular and consistent than the average gain of the control infants (group II).

The increased vitamin B intake in group II-B made little appreciable difference in the average weight and height when compared with those of the control babies, group II. Both the groups given supplementary vitamin B grew as well or better than the infants represented by standard growth curves. There was considerable superiority in the weight curve of the infants who received added vitamin B during 1934-1935 as compared with the curve representing the babies who received the diet fortified with vitamin B during the first year. This superiority is probably accounted for by the increased intake of milk in the second year and the earlier use of cereal, vegetables and fruit, as well as by a lower intake of vitamin D during the first year. For the same babies there is practically no difference in the average heights. From these results it is apparent that if one is to evaluate the effect produced by augmenting the intake of vitamin B the diet must contain an adequate and balanced amount of the other vitamins as well as an optimal amount of food.

Owing to the fluctuations that we have noted in the various components of growth, particularly in the control group, it is well to call

attention to the necessity of conducting such studies over a long period. Some of the conflict of opinions previously referred to may have arisen because the observations were made only for a comparatively short period.

Constipation was an infrequent complaint in the babies, so that the addition of vitamin B made no essential difference in its occurrence.

Severe vomiting was also a rare symptom and was found in only 2 infants in each group (with and without the vitamin B supplement).

Anorexia (refusal of the infant to take the prescribed amount of food) was found in almost the same number of infants whether or not they had additional vitamin B. Refusal of food for short periods during and after illness was found also in about the same number of infants in each group.

Infections of the respiratory tract or other areas were not reduced in number in the infants who were given the vitamin B supplement.

Eczema was infrequently found in all the groups.

The accomplishments of sitting alone, walking and saying words, as reported by the mother, do not appear to have been accelerated by the increase in the amount of vitamin B in the diet.

SUMMARY

This study on the nutritive value of evaporated milk fortified with vitamin B_1 in the form of an aqueous extract of rice polishings was conducted with 193 full term normal infants during the first year of life. At the beginning of the observations the babies ranged from 1 to 10 weeks of age, with an average of 5½ weeks, and weighed approximately 4 Kg. The 142 infants in groups I-B and II-B received from 90 to 100 Sherman-Chase units of vitamin B more per day than the 51 infants in group II, who served as controls. In the endeavor to measure the growth in numerous directions and to note changes in the infant's "plane of health," monthly observations were made. In these, 17 anthropometric measurements were made and the weight was determined; roentgenograms of the long bones and measurements by planimeter were made for the detection of rickets and scurvy and the determination of the type of bone formation; hematologic studies, including red cell, white cell and differential counts and determinations of the hemoglobin content, were made, and capillary resistance tests for the detection of scurvy were performed.

The efficiency of utilization of milk, as judged by dividing the average daily gain by the number of ounces (29.6 cc.) of reconstructed evaporated milk (1:1), became superior after the one hundred and twenty-sixth day of life for the infants who received the milk fortified with vitamin B.

An increase of from 30 to 50 per cent of vitamin B in a controlled formula of evaporated milk, water and corn syrup acidified by the addition of commercially dehydrated lemon juice powder produced a greater regularity of growth in infants, as judged by certain measurements. Group averages demonstrated fewer erratic fluctuations for the infants receiving the vitamin B supplement than for those not receiving it. It seems justifiable to interpret this study to indicate that increased amounts of vitamin B in the diets of infants aid in promoting a more stabilized growth and greater nutritional stability, as there is a general consistency in all the findings from the many types of observations, whether qualitative or quantitative, although the differences were small and there was a small difference in the number of infants in each group.

Twice the number of cases of mild diarrhea were observed in the infants receiving additional vitamin B in the form of an aqueous extract of rice polishings, which suggests a laxative effect of that extract. On analysis of the cases, however, it was found that the increased frequency of bowel movements was initiated by, or coincident with, an infection.

The average hemoglobin level for the infants receiving the vitamin B supplement seemed to be more constant after the customary initial drop of the first few weeks. While the values did not show a higher average level except in the later weeks of observation, they did not fluctuate as widely. This again demonstrates the possible stabilizing effect of vitamin B on growth and nutrition.

Senia Kangas, R. N., assisted in this study as director of the nursing service; Rachel Moore, as roentgen technician; Betty Munday, M.A., Louise Emerson, A.B., and Marion Lange Shepherd, A.B., as laboratory technicians; Francis Slyker, Ph.B., as statistician, and Helen A. Hunscher, Ph.D., and Rose V. Schwartz, A.B., as assistants in preparing the data for interpretation and publication.

RELATION OF INCREASED VITAMIN B (B_1) INTAKE TO MENTAL AND PHYSICAL GROWTH OF INFANTS

PRELIMINARY REPORT

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THOMAS B. COOLEY, M.D.
DETROIT

The relation of nutrition to mental and physical growth is still largely an unsettled question. Especially in the psychologic field, the few available studies on animals and human beings have produced conflicting results. With respect to vitamin B, Maurer and Tsai [1] reported that its lack in nursing rats results in a markedly diminished capacity for maze learning in the adult rats. Bernhardt [2] confirmed these data. On the other hand, Anderson and Smith [3] reported that maze learning in mature rats is not adversely affected by a diet deficient in vitamin B. Balkin and Maurer [4] reported a quantitative experiment on children aged from 5 to 9 years. Using several standardized "mental tests," they found that augmenting the vitamin B in the diet of a group of malnourished children produced striking improvement in the performance of every child in every test, and this in spite of the short period of the diet rich in vitamin B as compared with the long period of the

The expenses of this study were defrayed in part by a grant from the Borden Company through L. J. Auerbacher.

From the Genetic Psychology Laboratory of the University of Michigan, Ann Arbor, and the Research Laboratory of the Children's Fund of Michigan, Detroit.

1. Maurer, S., and Tsai, L. S.: The Effect of Partial Depletion of Vitamin B Complex upon Learning Ability in Rats, J. Nutrition **4**:507, 1931.

2. Bernhardt, K. S.: Effect of Vitamin B Deficiency During Nursing on Subsequent Learning in the Rat, J. Comp. Psychol. **17**:123, 1934.

3. Anderson, J. E., and Smith, A. H.: The Effect of Quantitative and Qualitative Stunting on Maze-Learning in White Rats, J. Comp. Psychol. **6**:337, 1926.

4. Balkin, E. R., and Maurer, S.: Variations in Psychological Measurements Associated with Increased Vitamin B Complex Feeding in Young Children, J. Exper. Psychol. **17**:85, 1934.

defective diet. Hoefer and Hardy [5] correlated the intelligence quotients of public school children with their early feeding methods and found that the children who had been breast fed between the ages of 4 and 9 months ranked first, that those artificially fed ranked second and that those entirely breast fed from the first to the twentieth month ranked lowest. Mother's milk is known to be deficient in vitamin B.[6] Such studies are purely indicative, in that they lack any semblance of necessary controls.

A unique opportunity for making psychologic observations in cases in which the physical factors were accurately known was offered by the comprehensive program of the Research Laboratory of the Children's Fund of Michigan for the study of growth. A brief description of the general program [7] involving vitamin B follows.

METHOD AND MATERIALS

The artificially fed infants lived in their own homes and were cared for by their parents. At the initial observation in the growth clinic all the babies were 2½ months of age or less—the minimum age was 5 days and the average age 5½ weeks. Approximately two-thirds were white and one-third Negro (or dark skinned), and many of the families were receiving help from the Detroit public welfare association.

A consistent effort was made to limit variables as far as possible throughout the observations, measurements and procedures. A basal formula of evaporated milk was chosen not only because it is consistent with present principles of pediatric practice but because the content and the quality of that milk could be kept constant for all groups studied and throughout an extended period. By incorporating a water extract of rice polishings at the time of making up a year's supply of evaporated milk, even distribution of vitamin B (B_1) strength could be insured. The fortified product contained from 2 to 2.7 Sherman-Chase units of vitamin B per gram of solids, whereas the nonfortified contained only from 0.7 to 1 unit. When the fortified milk was tested on rats, there was substantially a threefold increase in the vitamin B response, and there was little or no evidence of deterioration on storage for one year. As an aid to further standardization of the basal formula, lemon powder of an approximately constant quality, as a source of the antiscorbutic vitamin, and cod liver oil of the same source and potency as the antirachitic vitamin were used. Standardization of the caloric content was maintained by the use of corn syrup as the additional carbohydrate. Cereals low in vitamin value were added to the diet at the age of 5 months and strained vegetables (carrots, peas, potatoes and spinach) at 6 months. This basal diet furnished on the average 320 Sherman-Chase units of vitamin B daily for the infants receiving the milk fortified with an aqueous solution of vitamin B (B group) and 227 units for those receiving the nonfortified milk.

5. Hoefer, C., and Hardy, M. C.: Later Development of Breast Fed and Artificially Fed Infants: Comparison of Physical and Mental Growth, J. A. M. A. **92**:615 (Feb. 23) 1929.

6. Macy, I. G., and Outhouse, J.: The Vitamin Content of Milk Used in Infant Feeding, Am. J. Dis. Child. **37**:379 (Feb.) 1929.

7. The methods and procedure were described in detail in a recent report [8] since they served as the basis for a group of studies on growth, of which the present study is one.

PHYSICAL GROWTH

Under the aforementioned experimental conditions an effort was made to determine the nutritive advantage to the health, the related growth-promoting phenomena and the bone-building and body-building value of supplementary amounts of vitamin B in the form of a water extract of rice polishings.

Criteria for the estimation of the nutritive advantages were looked for in monthly medical examinations, which included determination of the weight and seventeen anthropometric measurements, hemoglobin estimations, red blood cell counts and examination of the long bones in roentgenograms and their measurement by planimeter. According to these observations, an increase of from 30 to 50 per cent in the intake of vitamin B appeared to produce more regular, though not consistently greater, growth in infants, as judged by the group averages of the various measurements. Increased amounts of vitamin B in the diet seemed to promote a more stabilized growth and greater nutritional stability.[8]

MENTAL GROWTH

If it appears from the data thus far statistically treated that there were few differences between the two groups as to the resultant gross bodily growth, it is perhaps significant that certain fine metabolic processes which may directly affect the nervous system were apparently affected, viz., the hemoglobin content and the efficiency of utilization of milk. Certainly, on the structural aspect of nerve tissues there is an increasing accumulation of experimental data. Though they do not always agree as to the specific cause and sometimes disagree as to the location, histologic studies converge at least on one point—that a diet defective in vitamin B is accompanied by serious pathologic changes in the nervous system. Earlier investigators stated that the effects are largely, if not exclusively, peripheral and that they are confined to degeneration of the myelin sheaths; recent studies, with improved technic, showed that serious degeneration takes place in the central fibers and nuclei. Both facts are of interest to the psychologist, since some correlation between pathologic nervous structures and pathologic behavior is practically inevitable. With severe forms of beriberi the correlation between behavior and degeneration of the tissue seems amply apparent in such symptoms as lethargy, the loss of the deep reflexes, paraplegia, anesthesia, distorted locomotion, paralysis of the legs and arms and the various other sensorimotor disturbances commonly described. The effects of

8. Poole, M. W.; Hamil, B. M.; Cooley, T. B., and Macy, I. G.: Stabilizing Effect of Increased Vitamin B (B_1) Intake on Growth and Nutrition of Infants: Basic Study, Am. J. Dis. Child., this issue, p. 726.

such pathologic changes on the higher mental processes are less well known and, as one would expect, more variable, although numerous observers have reported mental depression, followed by indifference and mental prostration, in adults and fretful, "infantile" crying and depressed perceptual capacity in children. Various investigators with animals have reported a similar caudal-cephalic paralytic spread, with a characteristic emotional *Unlust* accompanying it, in the various species studied. Bernhardt [2] suggested that with human beings, particularly, a diet defective in vitamin B "might mean decreased ability to respond to complex situations," rather than any obvious effect in the more primitive nervous levels.

It is obvious that practically all the histologic work and most of the behavior studies have concerned pathologic deficiency of vitamin B. In the present study we approached the problem from the opposite angle, by seeking to determine the effects, if any, of an increase of vitamin B in the diet in a group of normal infants. For a group of twenty-five infants on a diet containing augmented vitamin B, a total of sixty-five behavior items were observed under laboratory conditions at the age levels of 6, 9 and 12 months. These items include the Gesell and the Bühler-Hetzer normative tests, a selected group of representative deep and superficial reflexes and a few additional discrimination and learning tests. The data obtained were compared with similar data for two normal control groups of the same age and number, one from the ranks of the Children's Fund clientele and one from a group of nursing infants used as subjects in the Genetic Psychology Laboratory in Ann Arbor, Mich. While this "longitudinal" group is admittedly small for statistical validity, there is a compensation in having three sets of developmental data for the same infants over a period of six months. There were fourteen additional infants in the vitamin B group at the 12 month level and a few scattered infants at intervening age levels. For all age groups, additional control children were available from infants receiving a diet rich in vegetables.

A minute cross-comparison of each item for the various groups revealed the following general results:

At the 6 month level, the B group showed definite acceleration in fifty-nine of the sixty-four behavior items and equality in five. The range in superior scores extended from 2 per cent for some items to 48 per cent for others. The most striking differences occurred in the categories of visual pursuit, sustained fixation, eye-hand coordination patterns and prehension. Consistent *general* tendencies regardless of items were shorter reaction times, dominance of specific over "diffuse," or "irradiated," responses and accelerated coordination of the anterior postural reflexes. "Pure" plantar reflexes occurred more frequently

than in the control groups; fetal supine posture was less evident; there was less lag in spatial orientation to auditory and visual stimuli, and there was more accurate localization of tactile pressure. No differences were evident in the few sympathetic reactions recorded, viz., pupillary response to sharp or pinching tactile stimuli, pupillary reflexes to light and vasomotor and respiratory changes with strong or sudden stimuli. Extremely small favorable differences occurred in the locomotor reflexes of the legs as compared with the superior coordination of the head, neck, trunk and arms in an accelerated independent sitting posture.

The general picture of the infants receiving increased amounts of vitamin B may perhaps be qualitatively summarized as one of slightly accelerated maturation in basic behavior patterns (except the sympathetic), augmented alertness in attention and perception phenomena and slightly accelerated adaptive behavior patterns (learning). The psychologist's logical inference from these data is that some common factor acting with particular directness at this age level on the nervous system must account for the consistent qualities of sensorimotor behavior. These general qualities are speed, directness and plasticity of response, all of which could be accounted for speculatively by the mere mechanics of accelerated myelinization, especially in the rapidly developing pyramidal tracts, which are largely unmyelinated at birth. Histologic evidence for such an explanation, however, seems completely lacking, so it must remain for the present an interesting speculation.

Comparison at the 9 month level revealed the same general tendencies in the B group but showed a decrease in the number of superior item scores from fifty-nine to forty-six, as well as a decrease in the range of the superior scores. Marked individual differences in all groups at this level increased the size of the average deviation, thereby decreasing the significance of the mean performance. Regarded as a whole, however, the performance of the vitamin B group was still slightly superior to that of any of the control groups, with approximately the same distribution, or "profile," for the various items.

Comparative data for the groups at the 12 month level show evidence of further leveling; so the behavior of the infants on augmented intakes of vitamin B, while still accelerated, was only marginally so. Furthermore, several inconsistencies appeared, which at the present analysis are somewhat inexplicable. Thus, while the various types of prehensile reactions remained superior, the locomotor responses were slightly retarded. A second inconsistency occurred in the locomotor patterns. Thus, the basic reflexes as well as the various complex upright postural coordinations were alike in all three groups, but the very factor in which one would expect acceleration in the B group was strangely lagging at the 12 month level, namely, the independent effort to stand

alone without strong and usually personal support. In passing, it may be said that the older ideas of a high correlation between intelligence and precocious walking are largely invalidated at present; but this fact does not go far in explaining the actual lag in the B group at the age of 12 months.

Two further explanations may be offered, however, for the diminution in superior behavior at this age level. The one most closely related to this study concerns nutrition. Uniformity of diet and other physiologic factors which can easily be maintained at the age of 6 months are obviously more difficult to control or to analyze at 12 months, when nutrition is of necessity more varied and the metabolic picture thereby more complex. The other explanation concerns environmental influences which after the sixth or seventh month become so inextricably fused with the more native elements of maturational behavior that they are extremely difficult to control or even to isolate in "sampling" technics. The bulk of experimental work with infants seems more and more to indicate that at least after the age of 9 months "longitudinal" experiments from day to day, involving the basic processes of discrimination and learning within a unitary controlled situation, are a necessary superposition on the more general "sampling," or "test," procedures. Such an experiment, supplementing this preliminary study, would offer valuable evidence for the relation of vitamin B to the so-called higher mental processes.

As related to the foregoing experiment, two sets of incidental observations may be of interest. The same series of tests were later given to six normal infants aged from 3 to 4 months on a diet low in vitamin C and so regulated as to keep the infants barely above the line of pathologic deficiency. So far as this small group may be compared with the others, the following differences characterized its behavior: greater emotional instability (crying, irritability and long and difficult adaptation to the experimental situation), smaller range of individual differences (i. e., more homogeneous and stereotyped behavior patterns), lower average scores on the test series (c—), stereotypy of the Babinski-plantar sequence, retarded efforts at head lifting and longer reaction times to both visual and auditory stimuli, although visual fixation was equally well sustained. Beyond these items, there were no other apparent differences within this group, and the margin of difference, while consistent, was likewise small. Repetition of the tests after one month gave almost identical results.

Data from two cases of extreme infantile scurvy (age of the patient, 10 and 11 months, respectively) are incomplete because of the difficulty of handling infants so weak and so ill. For the thirty items recorded, chiefly sensory, prehensile and perceptual, the mental age of

the infants was certainly not beyond that of the healthy neonate or the typical year old congenital idiot. Fetal posture was almost uniformly held. Babinski extension alternated regularly with plantar flexion, but both were extremely feeble. Palsied shaking of the head or rapid lateral bobbing occurred throughout the experimental periods and was particularly violent after each new stimulus. Prickett [9] recorded exactly similar phenomena in his vitamin B-deficient rats immediately preceding the last stages of extreme spasticity. Pneumonia prevented repeated observations of the older child. Repetition of the tests on the 10 month old child after two and four weeks of medical treatment showed marked improvement, especially in postural ease and coordination, but with the total "score" only equivalent to that for the 4 month level.

All available data on vitamin B seem to indicate some close interaction in the infant between the metabolism and the development of external behavior. The nature of this interaction can be shown only by further and more highly controlled observations.

Ruth Gruitch and Constance Haas McMath, of Detroit, and Bing-Chung Ling, of Ann Arbor, rendered technical assistance in the observations on the various items.

9. Prickett, C. O.: The Effects of a Deficiency of Vitamin B_1 upon the Central and Peripheral Nervous Systems of the Rat, Am. J. Physiol. **107**:459, 1934.

RATE OF APPOSITION OF ENAMEL AND DENTIN, MEASURED BY THE EFFECT OF ACUTE FLUOROSIS

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Recent findings on the effect of fluorosis on the growing teeth of lower animals paved the way for this quantitative study of the rate of apposition of human enamel and dentin.

REVIEW OF THE DENTAL EFFECTS OF FLUOROSIS

Historical Summary.—For many years a type of hypoplasia of the enamel known as mottled enamel was a challenging problem to members of the dental profession. The condition was endemic and characterized by a destructive chalky opacity and pitting of the enamel. Black and McKay,[1] in 1916, first attempted to elucidate the underlying cause of this dental defect, and they were instrumental in initiating the large amount of research that followed. In 1931 Churchill suggested and Smith and her associates[2] established by experiments on animals that chronic fluoride intoxication was the direct cause of mottled teeth.

Churchill arrived at his discovery by a direct approach, when he analyzed the water in regions in which mottled enamel was endemic and found an unusually high content of fluorine present. He suggested that fluorine might be the cause of mottled enamel. Smith and her co-workers resorted to experimentation with animals and succeeded in reproducing the mottling of teeth in rats by adding to their diet concentrations of water from the communities in which mottling was endemic. Following a suggestion from a report by McCollum and Bunting, they were able to

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From the Department of Histology, University of Illinois College of Dentistry, and the Department of Pediatrics, University of Illinois College of Medicine, and the Research and Educational Hospital.

1. Black, G. V., and McKay, F. S.: Mottled Teeth: An Endemic Developmental Imperfection of the Enamel of the Teeth Heretofore Unknown in the Literature of Dentistry, Dental Cosmos **58**:129-156, 1916.

2. Smith, M. C.; Lantz, E. M., and Smith, H. V.: The Cause of Mottled Enamel, a Defect of Human Teeth, Technical Bulletin 32, University of Arizona, Agricultural Experiment Station, June 10, 1931.

reproduce the same condition by adding sodium fluoride to the diet. An analysis of the water from the affected communities revealed a high content of fluorine.

After proof was established that mottled enamel is caused by the toxic action of fluorides in water, the next step was to investigate the mechanism by which fluorine disturbed the teeth. Here again experimentation with animals proved to be necessary and enlightening.

Histologic Analysis.—The dental changes produced by injections of sodium fluoride into animals were studied. In the rat the injections produced sharp effects in the form of bands of defective pigmentation and calcification in the enamel. These changes could be seen with the naked eye, so that any one could tell the number of injections given to an animal by counting the bands on the surface of the enamel. Histologic analysis of the teeth showed corresponding bands of disturbed calcification in the dentin and in the enamel. In cross-sections these appeared in the form of concentric rings (fig. 1) similar to those seen in trees. Microscopic analysis showed that the effect of each injection consisted of an imperfect, hypocalcified layer followed by a secondary recovery reaction, which was evidenced as a normal or hypercalcified layer [3] (fig. 1).

The ameloblasts were the first cells to be affected. In rats, the effects could be recognized histologically in the enamel-forming cells within one hour after a single injection.[4] Since the cell was affected, the formation of the enamel was disturbed. The disturbance in calcification which occurred at the same time was probably brought about by the deposition of calcium fluoride in the tissue instead of the normal calcium salts (calcium phosphate or calcium carbonate) and possibly also by a disturbance of the enzymatic phosphatase system concerned in calcification.[5] The experimental observations thus showed that the effect of the fluorides was prompt and localized first in the formative organ of the tooth.[6]

The effec of chronic fluorine intoxication on development of bone, enzymatic action, body growth, respiration and reproduction are striking and destructive.[5a] These effects, however, are produced only by increased

3. Schour, I., and Smith, Margaret C.: The Histologic Changes in the Enamel and Dentin of the Rat Incisors in Acute and Chronic Experimental Fluorosis, Technical Bulletin 52, University of Arizona, Agricultural Experiment Station, June 15, 1934, pp. 69-91.

4. Schour, I., and Smith, M. C.: Injections of Sodium Fluoride on Enamel and Dentin of the Incisor of the Rat, Proc. Soc. Exper. Biol. & Med. **32**:1-2, 1934.

5. DeEds, Floyd: (*a*) Chronic Fluorine Intoxication: A Review, Medicine **12**:1-60 (Feb.) 1933; (*b*) Fluorine in Relation to Bone and Tooth Development, J. Am. Dent. A. **23**:568-574 (April) 1936.

6. Schour and Smith.[3] Schour and Smith.[4]

doses of sodium fluoride. The growing tooth is the first and the most delicate organ to react to the ingestion of fluorides.

A Method of Measuring the Rate of Growth.—The fact that each injection of sodium fluoride produced a distinct stripe in the enamel and the dentin which were forming and calcifying at the time it was given suggested a method for measuring the rate of apposition of these tissues. Measurements by micrometer between any two experimental stripes give the amount of apposition during the interval between the

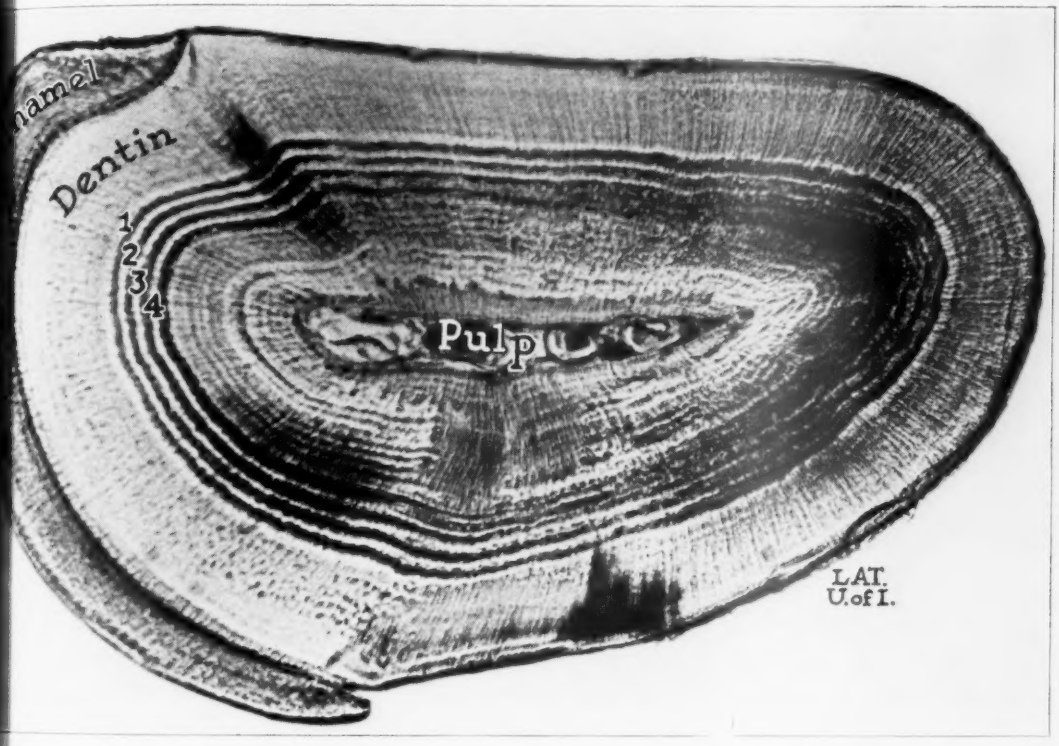

Fig. 1.—Photomicrograph of a transverse ground section of the incisor of a rat that was given four injections of sodium fluoride at forty-eight hour intervals and killed fourteen days later (× 45). The effects of the injections may be seen in the dentin as concentric incremental stripes of disturbed calcification 32 microns apart. This figure is reproduced from: Schour, I., and Smith, Margaret C.: The Histologic Changes in the Enamel and Dentin of the Rat Incisors in Acute and Chronic Experimental Fluorosis, Technical Bulletin 52, University of Arizona Agricultural Experiment Station, June 15, 1934, pp. 69-91.

two injections. The application of this method with a large group of animals of different species showed that the rate of apposition of enamel and dentin was consistently approximately 16 microns per

twenty-four hours in the smaller animals [7] and 4 microns per twenty-four hours in the Macacus rhesus monkey.[8]

These interesting observations on animals suggested the problem of determining the rate of apposition of enamel and dentin in the human being. An opportunity for studying this rate presented itself and made this investigation possible.

THE EMBRYOLOGY AND GROWTH PATTERN OF THE TOOTH

A brief review of the present knowledge of the developmental stages and growth pattern of human teeth will facilitate the evaluation of the results of this study (fig. 2). We shall use the deciduous central incisor for illustration (fig. 3).

The Tooth Germ.—The tooth is a derivative of the skin. It arises at the free margin of the jaws, primarily from an epithelial thickening, the dental anlage, or lamina (fig. 3 *A*). This epithelial base proliferates at its deeper end, invaginates and differentiates into the enamel organ (fig. 3 *B* and *C*). The cells that line the invaginated portion constitute the inner enamel epithelium (*I. e. e.* in figure 3). The remaining peripheral cells constitute the outer enamel epithelium (*O. e. e.*). The intervening portion consists largely of the stellate reticulum (*S. r.*) and a thin layer of stratum intermedium (*S. i.*) next to the inner enamel epithelium. The connective tissue which borders the invaginated portion condenses and forms the dental papilla (*D. p.*), the primordium of the dentin and the pulp. The boundary between the enamel organ and the dental papilla constitutes the future permanent dentino-enamel junction (*D. e. j.*).

Connective tissue cells arrange themselves about the outer surface of the enamel organ and the base of the dental papilla and form the dental follicle (*D. f.*), which will contribute to the formation of the cementum, the periodontal membrane and the alveolar bone. The tooth germ thus consists of the enamel organ, the dental papilla and the dental follicle (fig. 3 *C* and *D*). This stage is reached in the fourth fetal month.

The Enamel Organ.—The enamel organ does much more than its name implies. It would be more appropriate to call it the "odontogenic" organ. By its activity, it determines the size and the shape of the

7. Schour, I., and Hoffman, M. M.: Experimental Demonstration of the Daily Apposition of Sixteen Micra of Enamel and Dentin in Growing Mammalian Teeth, J. Dent. Research **15**:161-162, 1935.

8. Schour, I., and Hoffman, M. M.: The Rate of Apposition of the Enamel and Dentin in the Teeth of the Macacus Rhesus Monkey and the Rat as Measured by Means of Experimental Injection of Sodium Fluoride and Alizarine, to be published.

future crown and root. Its inner enamel epithelium, which consists of tall columnar cells, the ameloblasts, outlines the future dentino-enamel junction, is responsible for the formation of enamel, plays an active rôle in stimulating the underlying connective tissue cells to form the dentin of the crown and also joins the outer enamel epithelium to form Hertwig's epithelial sheath (*H. e. s.*), which guides the formation of the root (fig. 3 *E* and *F*). The connective tissue cells of the enclosed dental papilla which face the ameloblasts differentiate into the tall columnar odontoblasts (*Od.* in figure 3 *D*, *E* and *F*).

The Growth Pattern of Enamel and Dentin.—During the fifth fetal month the formation of the enamel and the dentin and the concomitant

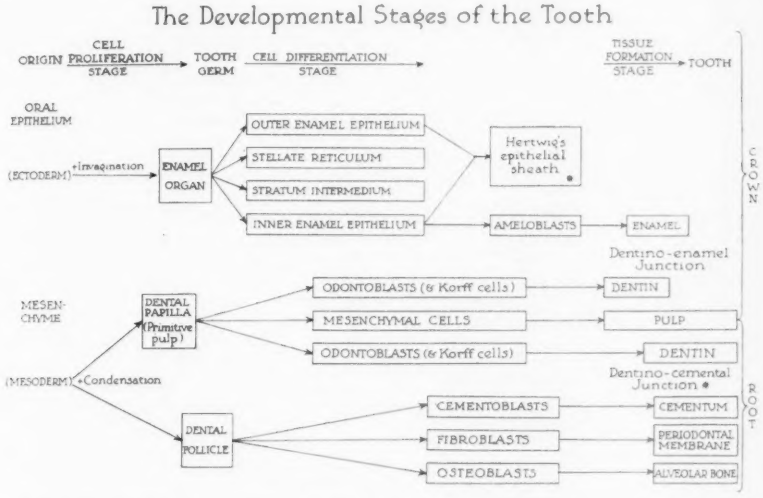

Fig. 2.—Chart showing the developmental stages of the tooth.

recession of the ameloblasts and the odontoblasts in opposite directions start at the highest point of the future dentino-enamel junction. Excepting for the formation of a microscopic cuspal portion of dentin, which precedes the formation of enamel (the black cap in figure 3 *D*, *E*, *F* and *G*), the deposition of enamel and that of dentin are synchronized so that for each layer of enamel that is apposed there is a corresponding layer of dentin. Incremental caps, or layers, of enamel are apposed one above another in an outward direction until the enamel reaches the full height of the cusp (fig. 3 *E* and *F*). The subsequent layers are apposed at the sides until the width of the tooth is established and the surface of the crown is complete (fig. 3 *F* and *G*). At the same time, incremental caps, or layers, of dentin are apposed one within the other at the expense of the enclosed pulp (fig. 3 *D*, *E*, *F* and *G*).

EXPLANATION OF FIGURE 3

A, primary stage of proliferation of the oral epithelium (*O. ep.*) forming the budlike dental anlage (*D a.*). This occurs at the sixth week of intra-uterine life for the deciduous central incisor.

B, secondary stage of epithelial proliferation and invagination, in which the cap-shaped enamel organ (*En. org.*) is formed. The condensation of the underlying mesenchymal tissue (*Mes.*) into the dental papilla (*D. p.*) may be noted; this occurs about the end of second month in utero.

C, stage of cell differentiation. The cells of the bell-shaped enamel organ and dental papilla (*D. p.*) are differentiated for their various functions; this occurs about the fourth month in utero.

D, primary stage in the formation of tissue. The formation of dentin takes place somewhat sooner than the formation of enamel. The first dentin cap (black) may be noted at the incisal tip. The permanent tooth bud (*P. b.*) is separated from its parent tooth germ and will undergo the same developmental stages. This stage occurs about fifth month in utero.

E, secondary stage in the formation of tissue. The enamel is apposed from within outward and the corresponding dentin from without inward. The development of Hertwig's epithelial sheath (*H. e. s.*), to guide the formation of the root, may be noted.

F, neonatal stage in the formation of tissue.

G, midsagittal view of the deciduous central incisor, showing the pattern of formation as represented by the incremental bands of Retzius, in the enamel, (striated portion) and the lines of contour, in the dentin. *N* and *n* represent accentuated incremental rings associated with the neonatal period. This stage is reached at the age of about 1 year.

H, transverse view through the gingival portion of the crown, as indicated by the arrow in *G*. The incremental bands of Retzius and the lines of contour resemble the concentric seasonal rings of trees.

The following abbreviations have been used: *Am.*, ameloblasts; *Al. b.*, alveolar bone; *Cem.*, cementum; *D. a.*, dental anlage; *Den.*, dentin; *D. e. j.*, dentino-enamel junction; *D. f.*, dental follicle; *D. l.*, dental lamina; *D. p.*, dental papilla; *En.*, enamel; *En. org.*, enamel organ; *H. e. s.*, Hertwig's epithelial sheath; *I. e. e.*, inner enamel epithelium; *Mes.*, undifferentiated mesenchyme; *N.*, neonatal ring in enamel; *n.*, neonatal ring in dentin; *Od.*, odontoblasts; *O. e. e.*, outer enamel epithelium; *O. ep.*, oral epithelium; *P. b.*, permanent tooth bud; *R. e.*, reduced enamel epithelium; *S. i.*, stratum intermedium, and *S. r.*, stellate reticulum.

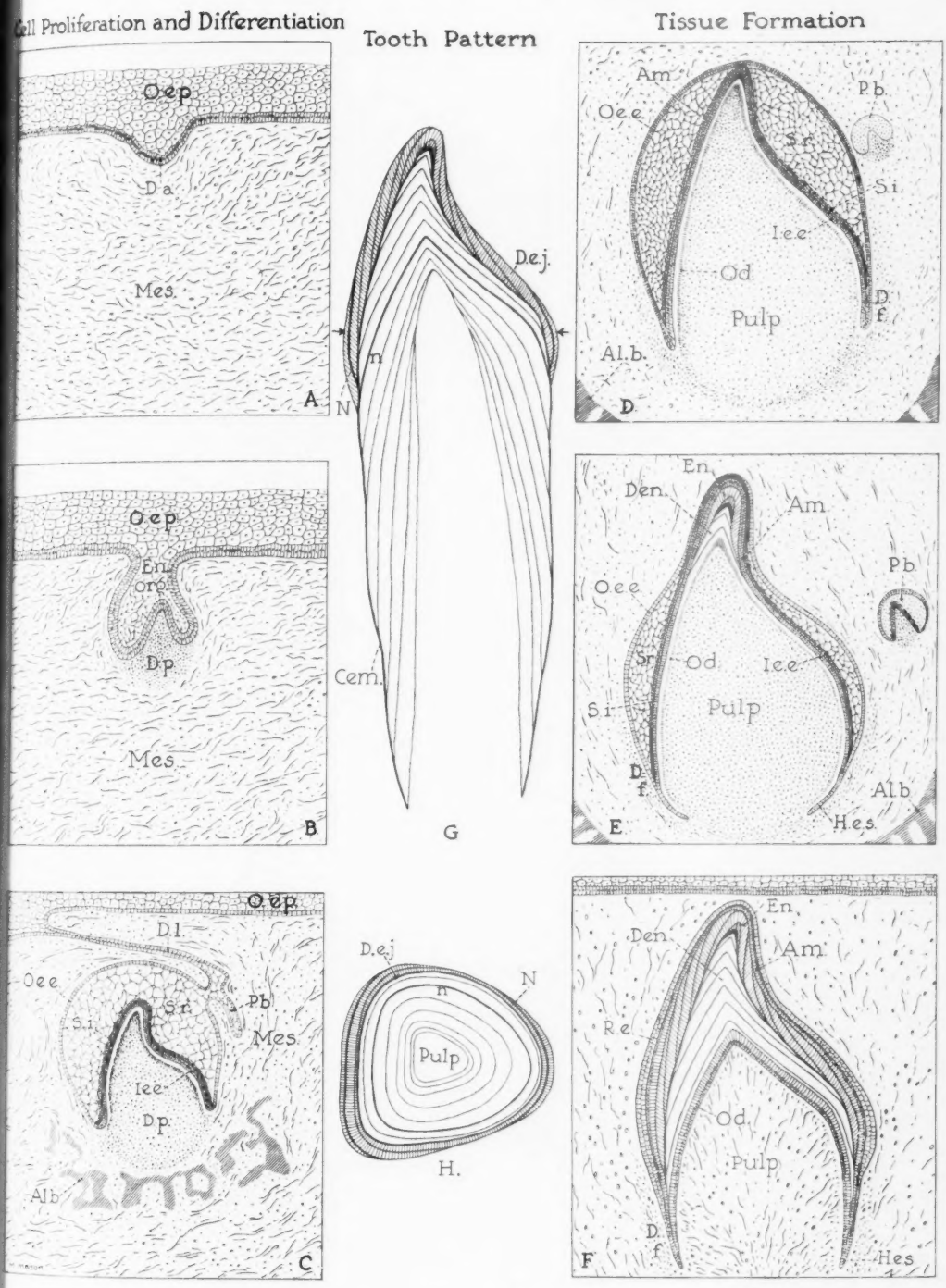

Fig. 3.—Embryology and growth pattern of the deciduous central incisor.

This process continues until the dentin of the crown and the root is completely formed. The process of calcification follows that of formation in close succession and accentuates the demarcations between successive incremental layers. These layers have been called bands of Retzius in the enamel (lines in the striated portion) and lines of contour in the dentin (fig. 3 *G* and *H*). The time of formation of any given incremental layer is in proportion to its distance from the dentino-enamel junction.

Since the apposition occurs in a regular and rhythmic manner, it creates a pattern of growth that is constant and characteristic for each type of tooth. Knowledge of this constant formative pattern, when combined with a quantitative knowledge of the rate of the formation, may lead to a mathematical concept of the growth pattern of each type of tooth, such as has been formulated for the incisor of the rat.[9]

The 16 Micron Rhythm.—Measurements by micrometer show that the normal increments, as represented by the bands of Retzius in the enamel and the lines of contour in the dentin, are approximately 16 microns wide.

This 16 micron incremental pattern was found to be normally present in the enamel and the dentin of many species, ranging from the rat to man.[10] By means of experimental injections of sodium fluoride [7] and alizarin, it was found to be a twenty-four hour phenomenon in the teeth of the cat and the dog and in the incisors of rodents and a four day phenomenon in the teeth of the Macacus rhesus monkey.[8] The time factor for human teeth is not known, and its determination was the chief object of this investigation.

MATERIAL AND METHODS

A 5 month old infant with inoperable hydrocephalus and meningocele was admitted to the ward. Despite the hopelessness of the affliction, he was otherwise normal. With the parent's permission, he was given one subcutaneous and twenty-four intravenous injections of from 1 to 2 cc. of 2.5 per cent sodium fluoride in sterile solution at intervals which ranged from three to nine and eight-tenths days, with the exception of one thirty-four and one-half day interval (table 1). The doses ranged from 3.8 to 7.6 mg. per kilogram of body weight. A total of 35 cc. of a 2.5 per cent solution of sodium fluoride, or 875 mg., was given over a period of one hundred and thirty days. The patient, therefore, received an average of 6.73 mg. of sodium fluoride per day. With this dose he showed no discomfort or reaction from the injections, made normal nutritional progress in growth and

9. Steadman, S. R., and Schour, I.: A Geometric Construction of the Rat Incisor, J. Dent. Research **15**:222-223, 1935.

10. Schour, I., and Hoffman, M. M.: Demonstration of a Sixteen Micra Rhythm in the Stratification of Enamel and Dentin in Man and Other Mammals, J. Dent. Research **15**:161, 1935.

development and was in good health until the age of 9 months, when he died as a result of confluent bronchopneumonia. The gross observations at autopsy and subsequent microscopic study of the tissues disclosed no evidence of any toxic action of sodium fluoride except in the dental tissues. Permission was obtained from the parents to resect the mandible and the upper central and lateral deciduous incisors for histologic study.

TABLE 1.—*Rate of Apposition of Enamel and Dentin, with Dose and Intervals Between Injections*

No. and Order of Injections	Dose, Cc. of 2.5 per Cent Solution of Sodium Fluoride	Interval Between Injections, Days	Dentin of Deciduous Central Incisor			Enamel of Deciduous Second Molar			Enamel of Permanent Teeth		
			No. of Measurements	Rate of Apposition per Interval, Microns	Rate of Apposition per 24 Hr., Microns	No. of Measurements	Rate of Apposition per Interval, Microns	Rate of Apposition per 24 Hr., Microns	No. of Measurements	Rate of Apposition per Interval, Microns	Rate of Apposition per 24 Hr., Microns
1.....	1.0	...	..	.....	....	..	.....	...	..	.....	....
2.....	1.0	9.0	55	38.06	4.23	..	.....	...	70	23.50	2.61
3.....	2.0	3.8	55	15.67	4.41	10	16.34	4.3	70	9.15	2.41
4.....	2.0	5.0	55	20.71	4.14	10	18.00	3.6	70	11.80	2.36
5.....	1.0	3.0	55	13.16	4.39	15	12.90	4.3	70	8.76	2.92
6.....	1.0	3.1	55	13.50	4.35	15	12.40	4.0	70	8.81	2.80
7.....	1.5	3.0	55	13.05	4.35	15	12.90	4.3	70	8.23	2.74
8.....	1.5	3.1	55	13.70	4.42	15	12.40	4.0	70	9.13	2.95
9.....	1.0	34.5	55	137.38	3.98	10	145.00	4.2	50	95.70	2.77
10.....	1.0	2.9	55	10.80	3.72	15	11.00	3.8	70	8.12	2.80
11.....	1.5	3.0	55	10.05	3.35	15	10.80	3.6	70	8.37	2.79
12.....	1.5	2.8	55	9.30	3.32	15	10.40	3.7	70	7.47	2.65
13.....	1.0	3.0	55	10.33	3.45	15	10.80	3.6	70	8.15	2.70
14.....	2.0	2.8	55	9.62	3.43	15	10.40	3.7	70	7.65	2.71
15.....	1.5	9.8	55	31.60	3.22				70	26.62	2.72
16.....	1.0	4.3	55	18.57	3.71				70	13.64	2.73
17.....	1.5	4.8	55	16.22	3.38				70	13.31	2.80
18.....	1.5	5.0	55	15.22	3.24				70	12.30	2.61
19.....	1.5	5.0	55	15.80	3.16				70	13.34	2.67
20.....	1.5	4.3	55	13.59	3.16		Not present		70	11.83	2.75
21.....	1.5	3.7	55	13.68	3.79				50	10.32	2.80
22.....	1.5	3.4									
23.....	1.5	3.7	Not measured						Not measured		
24.....	1.5	3.1									
25.....	1.5	3.2									
25 Totals	35.0	130.0	1,100		3.77	165		3.92	1,360		2.71

Before the tissues were removed, they were fixed by perfusion with a 10 per cent dilution of solution of formaldehyde U. S. P. Roentgenograms were taken previous to decalcification (fig. 4). One ground section of the deciduous upper right central incisor was prepared (fig. 5 *A*). The rest of the teeth and their investing tissues were decalcified, dehydrated, embedded in pyroxylin, cut in serial sections and stained with hematoxylin and eosin, Mallory's triple connective tissue stain, eosin and azure and alizarin.

A total of 2,625 measurements of these sections were made by means of a filar micrometer. In most instances a 4 mm. objective was used. Similar fields were measured by four different observers. The distance between any two suc-

cessive stripes studied was measured along the direction of the dentinal tubules or enamel rods, the path along which growth occurs. Since a gradient was found which varied with the region of the tooth, care was taken to make a proportionate number of measurements in every region of the tooth examined.

RESULTS

Histologic Observations on the Dentin.—Ground Section: In the dentin, the ground section of the deciduous upper central incisor showed the most distinct responses to each injection (fig. 5 *B* and *C*). Our quantitative observations on the rate of apposition of dentin are therefore based solely on this preparation.

A preliminary study was first made without the knowledge of the experimental history. Our estimate of the number of injections and the relative proportion of time that elapsed between them conformed closely with the experimental data and, as a test, indicated the efficacy of the method.

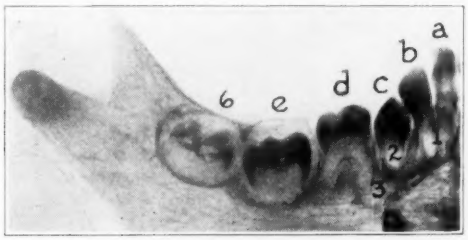

Fig. 4.—Composite roentgenogram of one half of the mandible of the infant at the age of 9 months (natural size). The following deciduous teeth may be seen: the central incisor (*a*), the lateral incisor (*b*), the cuspid (*c*), the first molar (*d*) and the second molar (*e*), as well as the first permanent molar (*6*). The position of the permanent central incisor, the lateral incisor and the cuspid is indicated by the figures *1*, *2* and *3*, respectively.

Figure 5 *B* and *C* shows that for each injection there was a distinct marking in the tooth in the particular portion that was forming and calcifying at the time of the injection. Since the patient was 5 months old at the beginning of the experiment, these effects were observed only in the root. The effects of the injections were seen as cleancut lines which were primarily disturbances in calcification. The dentinal tubules showed no deviation or bending when the injection was taking effect. This fact indicates that there were probably no disturbances in the formation of dentin.

Table 1 gives the average distance in microns and the time that elapsed between the formation of any two given lines. The average rate of apposition was calculated on the basis of twenty-four hour intervals. For the dentin of the deciduous upper central incisor, the

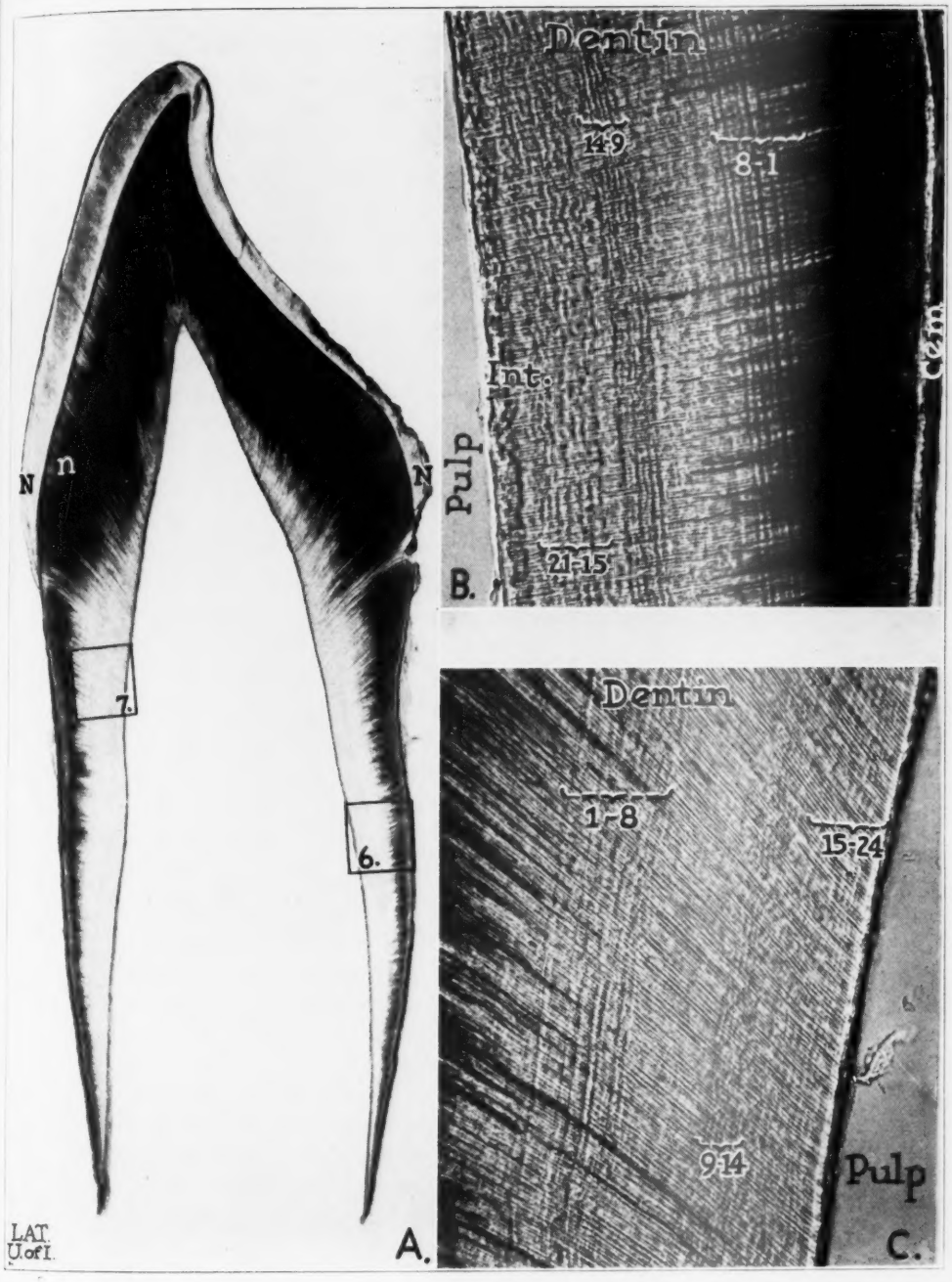

Fig. 5.—Photomicrograph of a ground section (× 10). This section was prepared by Dr. D. D. Jackson. Under higher magnification, the effects of the injections of sodium fluoride may be seen as incremental lines of disturbed calcification in the root portion of the tooth (*B* and *C*). *N* indicates the neonatal ring in the enamel, and *n*, the neonatal ring in the dentin. *B* is a magnified view of the lingual portion of the root as indicated at the right in *A* (× 100). The effects of the injections are seen as sharp lines of disturbed calcification. Lines 1 to 21 may readily be seen and are indicated in chronological order. Lines 22 to 25 are obliterated by interglobular dentin (*Int.*). *Cem.* indicates cementum. *C* is a magnified view of the labial portion of the root as indicated at the left in *A* (× 100). Lines 1 to 21 may readily be seen.

average rate of apposition calculated for the various intervals between injections ranged from 3.16 to 4.42 microns per twenty-four hours. The total average was 3.77 microns, with a standard deviation of 0.665 and a probable error of 0.013. In figure 6, a histogram, *A*, shows the range of 1,100 measurements on the rate of apposition in the dentin.

The first twenty-one injection lines appeared distinct and were easily measurable. The last four lines were less distinct because of diffuse distribution of interglobular dentin. Their intervals were therefore not recorded, although, when measured, they conformed with those of the preceding lines.

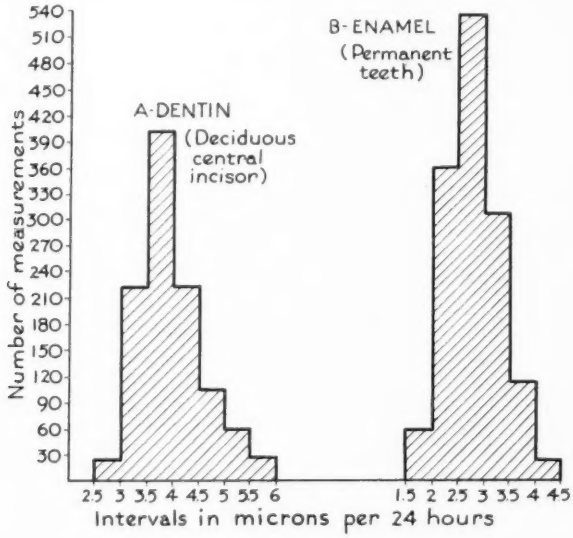

Fig. 6.—A histogram showing, *A*, the range of 1,100 measurements on the rate of apposition of the dentin in the deciduous central incisor and, *B*, 1,360 measurements of the enamel of the permanent teeth.

A comparison of the measurements of the average rate of apposition of the dentin in the various portions of the tooth indicates a definite gradient that appears to decrease as one proceeds from the dentinoenamel or the dentinocemental junction toward the pulp (table 1, intervals 1 to 21). It also decreases as one proceeds from the coronal to the apical portion of the tooth. In general, there appeared to be a correlation between the gradient and the form and the contour of the tooth.

Decalcified Sections: In decalcified sections, the dentin showed indications of the experimental stripes produced by the injections of sodium fluoride, but these stripes were not distinct enough to permit careful analysis and measurement. A histologic experiment was conducted

to determine the possible reason why in the decalcified sections the stripes did not show the distinct and sharp outline seen in the ground preparation. Only one half of the deciduous upper central incisor was used for the preparation of the ground section. The other half was decalcified, sectioned and stained. The loss of distinctness of the stripes in the decalcified portion indicates that the disturbances in calcification were obliterated to a large extent during the process of decalcification. This was not the case with the organic enamel matrix (fig. 7).

Histologic Observations on the Enamel.—Decalcified Sections: All the enamel of the deciduous teeth except the gingival portion of the second molar was fully formed and calcified at the end of the experiment and was therefore lost in the process of decalcification. The effect of the injections was observed only in the permanent teeth and in the gingival part of the deciduous second molar. Decalcified sections were cut labiolingually and mesiodistally. The lines produced by the first twenty-one injections were plainly seen and readily measurable (fig. 7). In many instances the effect of the last four injections was faint or obliterated by the staining reaction.

The direction of the enamel rods appeared to be stunted and interrupted after each injection (fig. 7). The resulting waviness and twisting of the rods indicated a disturbance in formation.

The Enamel of the Deciduous Second Molar: Most of the enamel of the second molar was completely formed and calcified before the first injection was given. After decalcification only a small portion at the gingival margin remained to show the effects of the first fourteen injections. A relatively smaller number of measurements, therefore, were made on this tooth. The average rate of apposition for the various injection intervals ranged from 3.6 to 4.3 microns per twenty-four hours. The total average was 3.92 microns per twenty-four hours, with a standard deviation of 0.26 and a probable error of 0.01 micron.

The Enamel of the Permanent Teeth: The effects of the injections were seen in the enamel of all the permanent teeth except the bicuspids and the second and third molars, which had not yet begun to form. The measurements showed an average rate of apposition for the various injection intervals ranging from 2.36 to 2.95 microns per twenty-four hours. The total average was 2.71 microns per twenty-four hours, with a standard deviation of 0.53 and a probable error of 0.009. Figure 6 *B* shows the range of 1,360 measurements on the rate of apposition of the enamel of the permanent teeth.

A comparison of the measurements of the enamel of the various permanent teeth which had appeared indicates a gradient that decreases consistently as one proceeds from the incisors to the cuspid and the

EXPLANATION OF FIGURE 7

A, a portion of the lower left permanent central incisor as indicated in the sketch at the left. This section was decalcified and stained with hematoxylin and eosin. The effects of the injections of sodium fluoride may be seen as incremental lines of disturbed formation and are numbered in chronological order. The staining had obliterated the effects of the last injections. The sharp bending of the enamel rods after each injection is noteworthy. No effects of the first eight injections are evident because this portion of the enamel did not begin to form until after those injections had been given. *Am.* indicates ameloblasts; *D. e. j.*, dentino-enamel junction, and *R. e. e.*, reduced enamel epithelium.

B, a portion of the organic enamel matrix of the lower right first permanent molar as indicated in the sketch at left. This section was decalcified and stained with alizarin. The effects of the injections of sodium fluoride may be seen as incremental lines of disturbed formation and are numbered in chronological order. The sharp bending of the enamel rods after each injection is noteworthy. The effects of the last four injections were obliterated by the staining reaction. *Am.* indicates ameloblasts showing intracellular globules, and *R. e. e.*, reduced enamel epithelium.

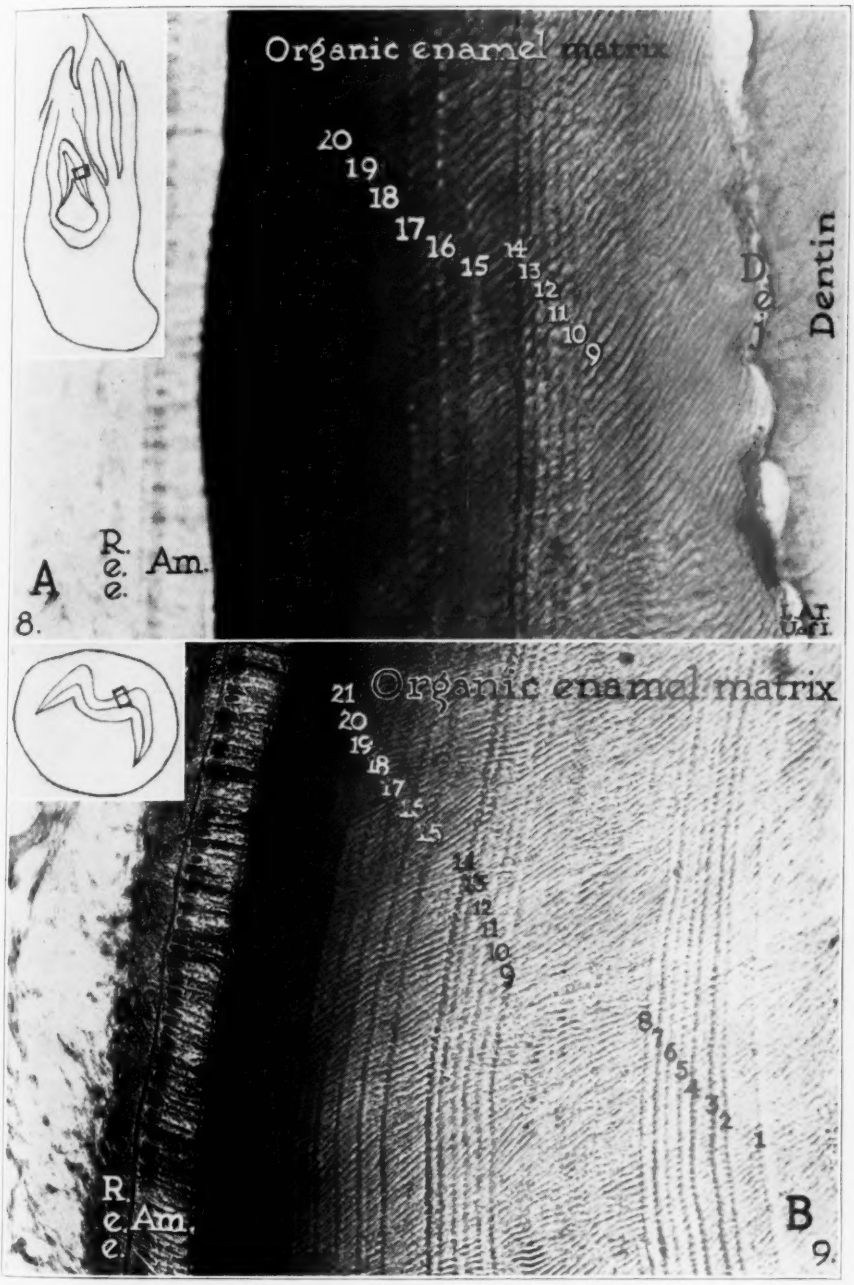

Fig. 7.—Photomicrographs of the organic enamel matrix (× 240).

first molar (table 2). A comparison of the various measurements of the enamel in any given tooth indicates a gradient that decreases consistently as one proceeds from the cusp to the gingival portion (table 2).

Ground Section: The enamel in the ground section of the deciduous upper central incisor showed no effects of the injections, since it was completely formed and calcified before the injections were given.

Changes in the Enamel Epithelium: The ganoblasts showed a number of fine hematoxylin-staining globules (fig. 7 *B*). These globules may have been the effect of the last injection and may be comparable to those seen in the ganoblasts of rats which were killed within one hour after an injection of sodium fluoride.[4] Enamel hypoplasia, consisting of an arrest in the formation of enamel and cysts in the enamel epithelium, was seen in the anterior permanent incisors. These changes were not severe and were probably associated with either the injections of fluorine or the hydrocephalic condition.

TABLE 2.—*Average Rate of Apposition of the Enamel in the Lower Permanent Teeth, in Microns Per Twenty-Four Hours*

	Central Incisor	Cuspid	First Molar
Cusp or incisal level	3.10	2.80	2.70
Gingival level	2.70	2.60	2.50
Total for entire tooth	2.90	2.70	2.60

Neonatal Rings.—The ground section of the deciduous upper central incisor showed a prominent stripe in the dentin, in the region of the crown, that had been formed previous to the first injection (figs. 5 *A* and 8 *A*). The distance between this dentin line and the line produced by the first injection averaged 520 microns. This distance, divided by 4 microns (the approximate average rate of opposition of dentin in that region per twenty-four hours for the first ten injections, table 1) gave us the number of days that had elapsed between the formation of the line in question and the date of the first injection. The calculated date was found to be the date of birth of the patient. In the gingival third of the enamel there was a prominent incremental line which corresponded in time of deposition with the prominent dentin line (fig. 8 *A*). These lines, therefore, were of neonatal origin.

Decalcified sections of all the deciduous teeth showed that the dentin that was formed and calcified previous to the neonatal stripe took a much deeper hematoxylin stain than the dentin formed and calcified subsequently (fig. 8 *B*). This difference in staining reaction indicates better prenatal than postnatal calcification.

These lines are ringlike in appearance in transverse sections or in three dimensions.

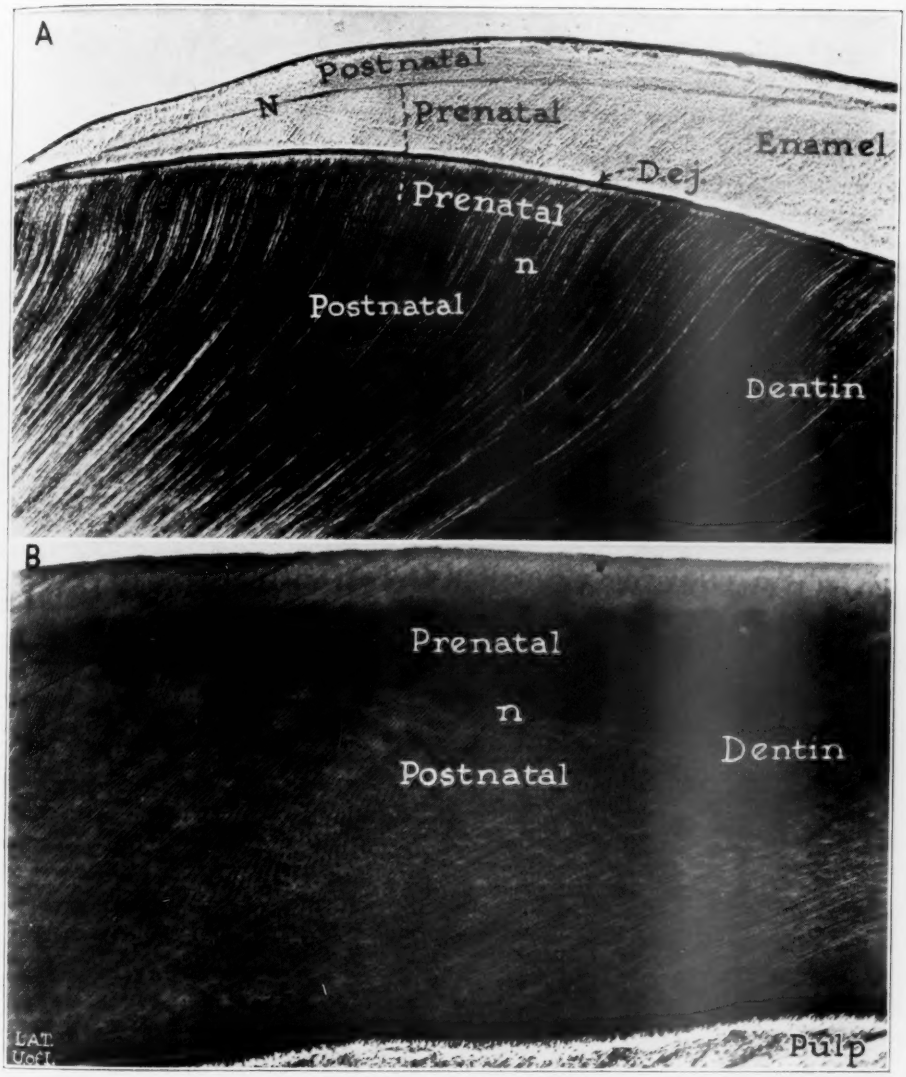

Fig. 8.—*A*, a magnified view of the labiogingival portion of the ground section of the incisor shown in figure 5 (× 66). The neonatal ring in the dentin (*n*) and the corresponding line in the enamel (*N*) are noteworthy. *D. e. j.* indicates the dentino-enamel junction. *B*, a photomicrograph showing the gingival portion of the dentin of a decalcified section of the deciduous upper lateral incisor (× 95). This section was stained with hematoxylin and eosin. The neonatal ring (*n*) demarcates the heavier staining, prenatal dentin from the lighter-staining, postnatal dentin. The enamel was lost during decalcification.

COMMENT

Validity of Our Observations as Indicative of Normal Processes.—The infant exhibited normal body growth, eruption of teeth and metabolic processes. The autopsy revealed no somatic disturbances except for the hydrocephalus and meningocele. The dose of sodium fluoride used was sufficient to produce the dental changes described but produced no general toxic symptoms of fluorosis. Our observations on the rate of growth, therefore, gave us valuable clues as to what we might expect under entirely normal conditions. This is especially true in connection with the dentin.

Differences in the Response to Fluorine.—The dentin showed no deviations in the direction of its tubules or other indications of an arrest in formation. The histologic experiment further indicated that the response in the dentin to the injections of fluorine was primarily one of a disturbance in calcification.

In the enamel, however, the sharp bending of the enamel rods at the time of the injections (fig. 7) and the presence of enamel hypoplasia indicated an arrest in formation in addition to a disturbance in calcification. The primary effect of acute fluorosis in the human being is probably on the enamel-forming cells, just as it is in the rat.[4] The enamel is apparently more sensitive than the dentin to fluorides. This may explain the fact that Black and McKay[1] in their histologic examination of mottled teeth found changes in the enamel but not in the dentin.

Possible Basis for the Gradient Indicated in the Measurements.—The slight but consistent variations in the measurements of the enamel and the dentin from the average rate of apposition in different regions appear to correspond with the particular form and contour of a given portion of the tooth (tables 1 and 2).

The fact that the curvature of the tooth makes it difficult to avoid cutting sections at slightly tangential planes should be considered in the evaluation of our data. Our observations, nevertheless, suggest the possibility that we are dealing with a definite gradient of growth and are in harmony with the following statement of D'Arcy Thompson:[11]

> A very large part of the specific morphology of the organism depends upon the fact that there is not only an average rate of growth common to the whole, but also a variation of rate in different parts of the organism. The smallest change in the relative magnitudes of these partial or localized velocities of growth will soon be manifested in more and more striking differences of form.

Our observations do not indicate any intervals of remission or rest in the formation of enamel and dentin for the period observed. The

11. Thompson, D'Arcy: Growth and Form, London, Cambridge University Press, 1917.

interval between the ages of 5 and 9 months, the period studied in this case, may be one of the active and continuous periods of growth. This problem of the gradient and the chronology of growth and rest periods awaits the accumulation of considerable material concerning different and longer age periods before it can be solved satisfactorily.

The Neonatal Ring.—The significance of our finding of a neonatal ring in the enamel and the dentin of the deciduous teeth depends on whether this ring was an isolated occurrence in our subject or constitutes a constant phenomenon occurring in all or most human deciduous teeth. An analysis of over 350 human deciduous teeth chosen at random showed that a neonatal ring was present in the enamel and the dentin in 90 per cent of the teeth.[12] In a large proportion of these teeth there was a distinct difference in the appearance of the staining reaction between the prenatal and the postnatal enamel and dentin. Both ground and decalcified sections indicated a better prenatal than postnatal calcification.

One may regard the neonatal ring as a permanent biologic landmark which mirrors the metabolic changes that the child experiences in its adjustment from intra-uterine to extra-uterine existence.

Delicacy of the Response of the Teeth.—Erdheim[13] pointed out that the dentin of the incisor of the rat is so delicate in its response to disturbances in the calcium metabolism that it acts like a drum of a kymograph on which are recorded the vacillations in the calcium metabolism in a clear and easily readable manner. Our present findings show that Erdheim's analogy not only applies to the dentin of the incisor of the rat but applies equally to both the dentin and the enamel of human teeth when they are growing and calcifying. It may be justifiable to consider the human teeth as teeth of continuous growth, with this important qualification, that the factor of continuous growth applies to that portion of the life span of the human tooth which covers its period of active growth.

SUMMARY AND CONCLUSIONS

The effects of injections of small doses of sodium fluoride on growing teeth were studied in a hydrocephalic infant between the ages of 5 and 9 months. The dose varied from 1 to 2 cc. of a 2.5 per cent solution. The medical history and the observations made at autopsy showed no general toxic effects of fluorosis. A histologic analysis yielded the following observations:

12. Schour, I.: The Neonatal Line in the Enamel and Dentin of the Human Deciduous Teeth and First Permanent Molar, J. Am. Dent. A. **23**:1946-1955 (Oct.) 1936.

13. Erdheim, J.: Ueber die Dentinverkalkung im Nagezahn bei der Epithelkörperchentransplantation, Frankfurt. Ztschr. f. Path. **7**:295-342, 1911.

1. The dentin showed a stripe of disturbed calcification and the enamel showed a stripe of disturbed growth and calcification in the portion of the tissue which had been forming and calcifying at the time of each injection.

2. The average rate of apposition of the dentin in the root of the deciduous upper central incisor, based on 1,100 measurements of the distance between successive injection lines, was 3.77 microns per twenty-four hours.

3. The average rate of apposition of the enamel in the gingival portion of the deciduous lower second molar, based on 165 measurements, was 3.92 microns per twenty-four hours.

4. The average rate of apposition of the enamel of the permanent teeth present, based on 1,360 measurements, was 2.71 microns per twenty-four hours.

5. Slight but consistent deviations from the average rate of apposition were observed; they appeared to correspond with the particular form and contour of a given tooth. These deviations are indicative of a definite gradient of growth for each type of tooth.

6. In the deciduous teeth, a distinct ring of disturbed calcification was found in the enamel and the dentin which were formed at and soon after birth. These rings are regarded as the neonatal rings in the enamel and the dentin and constitute a landmark which separates the prenatal and the postnatal portions of the deciduous teeth. The histologic analysis indicated better prenatal than postnatal calcification.

An experimental method is presented whereby further light may be thrown on a number of phases of the normal processes of formation and calcification of the teeth. It is hoped that similar collaborative studies will be conducted.

HUMAN PASSIVE TRANSFER ANTIBODY

II. NEUTRALIZATION OF ANTIGEN

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Since publication of the results of the experiments of Prausnitz and Küstner in 1921,[1] many investigators have studied the behavior of mixtures of allergic serum and antigen. The evidence indicates that serum capable of conferring passive local sensitization conforms in many respects to the characteristics of an antibody; such serum may be neutralized by its specific antigen, either in vivo or in vitro or possibly in both. Neutralization of antigen by its specfiic passive transfer antibody has been observed,[2] but the conditions which are necessary for its demonstration appear to warrant further investigation.

In several investigations,[3] mixtures containing arbitrary amounts of serum and antigen were used without due regard to the quantitative relationships involved. Jadassohn [2a] clearly pointed out that properly planned antigen neutralization experiments require concentrations of antigen within the neutralizing capacity of the serum used.

The method of titration of antibody described by Woringer [4] and further defined and developed by us [5] provides a means of estimating the potency of sensitizing serum by determining the minimal amount of antigen, in milligrams of total nitrogen per cubic centimeter, neces-

From the New York Hospital and the Department of Pediatrics, Cornell University Medical College.

1. Prausnitz, C., and Küstner, H.: Studien über die Ueberempfindlichkeit, Centralbl. f. Bakt. (Abt. 1) **86**:160, 1921.

2. (*a*) Jadassohn, W.: Allergiestudien bei der Ascaridenidiosyncrasie, Arch. f. Dermat. u. Syph. **156**:690, 1928. (*b*) Harley, D.: Hay Fever: I. A Study of Reagin-Allergin Mixtures, Brit. J. Exper. Path. **14**:171, 1933.

3. (*a*) Levine, P., and Coca, A. F.: Studies in Hypersensitiveness: XX. A Quantitative Study of the Interaction of Atopic Reagin and Atopen, J. Immunol. **11**:411, 1926. (*b*) Storm van Leeuwen, W., and Kremer, W.: Uebertragungs- und Hemmungssubstanzen im Blute von Allergikern, Ztschr. f. Immuntätsforsch. u. exper. Therap. **50**:462, 1927. (*c*) Kremer, W.: Uebertragungs- und Hemmungssubstanzen im Blute von Allergikern, ibid. **78**:382, 1933.

4. Woringer, P.: Méthode de dosage de l'anticorps ovalbumique dans le sang des sujets allergiques au blanc d'oeuf., Ann. Inst. Pasteur **50**:270, 1933.

5. Lippard, V. W., and Schmidt, W. M.: Human Passive Transfer Antibody: I. Titration by Neutralization, Am. J. Dis. Child. **54**:288 (Aug.) 1937.

sary for complete neutralization or slight overneutralization of the antibody. In this way the minimal concentration of antibody in a given serum may be expressed in terms of antigen equivalence. This provides an investigative approach to the problem of antigen neutralization in serum-antigen mixtures prepared so as to contain an excess of antibody. If antigen neutralization does occur, one may expect to demonstrate it in such mixtures.

This report presents the results of studies with such serum-antigen mixtures to determine, if possible, the ability of the passive transfer antibody to neutralize its specific antigen as evidenced by the reactions induced by injections of such mixtures into naturally or artificially sensitized skin.

TABLE 1.—*Titration of Passive Transfer Antibody According to Method of Neutralization*

Number	Ragweed, Nitrogen per Cc. in Serum-Antigen Mixture (Intracutaneous Injection), Mg.	Reaction Following Intramuscular Injection of Ragweed Antigen (0.3 Mg. of Nitrogen per Cc.) 24 Hours Later
1	0.015	0
2	0.006	0
3	0.003	0
4	0.0015	0
5	0.0006 (selected for neutralization experiment)	+
6	0.0003	+
7	0.00003	+

METHOD AND MATERIAL

Since it is necessary to know the passive transfer antibody titer of the serum to be used, the method of titration will be briefly outlined before the procedure of the neutralization tests is discussed.

Titration of Passive Transfer Antibody.—The technic was described in detail in the preceding paper.[5] Briefly, a series of mixtures was prepared, each containing 0.4 cc. of serum and 0.1 cc. of a saline dilution of antigen.[6] The final antigen concentrations of the mixtures are shown in table 1. Each mixture of the series (0.1 cc.) was injected intracutaneously into each of three recipients. Twenty-four hours later an intramuscular injection of antigen was given. The degree of reaction at the sites of the intracutaneous injections was recorded, and the titer was read from the antigen nitrogen concentration of the mixture used at the first nonreacting site.

Preparation of Mixtures.—The suitability of a serum for these studies, as well as the concentration of antigen to be used, was judged by the result of preliminary antibody titration. A serum of relatively low antibody titer could not be used, for

6. The Arlington Chemical Company, Yonkers, N. Y., supplied many of the antigens used in these investigations.

the highest concentration of antigen within its titration level would not be strong enough to give appreciable cutaneous reactions. Therefore, serums of relatively high titer were selected, and the mixture containing the strongest or next to the strongest antigen concentration within the titration level was chosen for the subsequent procedures.

Three mixtures, comprising antigen plus specific serum, unrelated serum and saline solution, respectively, were prepared. The specific serum was the untreated test serum. The unrelated serum was the serum of another allergic person with passive transfer antibody of equal titer against another antigen but of none against the antigen used. The final concentration of antigen nitrogen was the same in all mixtures.

The mixtures were stored in the refrigerator for twenty-four hours before being used. A few, stored at room temperature, gave the same results.

Subjects.—The tests were performed either on the naturally sensitive skin of allergic persons (e. g., a patient with ragweed hay fever was used for ragweed tests) or on locally sensitized cutaneous areas of normal recipients, which had been prepared twenty-four hours previously (in some instances, forty-eight or seventy-two hours previously) by intracutaneous injections of 0.1 cc. of undiluted sensitizing serum. The recipients included both children and adults. The children were all over 4 years and averaged 9 years.

Tests.—In the earlier observations the tests were made with 0.025 cc. of the mixtures injected with a 1 cc. tuberculin syringe. In order that we might obtain smaller controls for more distinct differentiation, the later tests were made with 0.01 cc. injected with a 0.25 cc. tuberculin syringe. The reactions were measured fifteen minutes after the injections and were traced on cellophane in several instances. To control variations in the reactivity of different cutaneous sites, the position of the tests was reversed in each of the two recipients. The response of the skin to the intracutaneously injected mixtures was judged chiefly by the size of the wheals produced. Reactions differing from the controls by 2 mm. or less were considered negative. We attached less significance to the erythema, but in general this was of greater magnitude as well as of greater intensity in the positive reactions. This is in accord with the experiments of Lewis,[7] who concluded that either the extent and the brightness of the "flare" or the prominence of the wheal may serve as a gage of the strength of the stimulation. Since the intensity of erythema is difficult to estimate quantitatively and its extent is often ill defined, the wheal was regarded as the more reliable indicator.

Controls.—In all instances, the response to the intracutaneous injections of the test mixtures was controlled. In the case of naturally sensitive recipients, the specific and unrelated serum-antigen mixtures were controlled by intracutaneous injections in comparable areas of skin of the same quantities of serum. In the case of artificially sensitized recipients, the three test mixtures were controlled by concurrent injection of the identical mixtures into comparably located unsensitized areas of skin.

RESULTS

Table 2 shows the results of a typical observation on a naturally sensitive recipient, and the reactions are graphically represented in figure 1. It may be seen that the reaction to the specific serum-ragweed

7. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927, p. 72.

mixture was not appreciably larger than that to its serum control. The reaction to the unrelated serum-ragweed mixture was considerably larger than that to its control, and the reaction to the saline solution-ragweed mixture was considerably larger than that to either serum control. Finally, the reaction to the saline solution-ragweed mixture and that to the unrelated serum-ragweed mixture were both notably larger than that to the specific serum-ragweed mixture.

Table 3 shows the results of a typical observation on an artificially sensitized recipient, and the reactions are graphically represented in figure 2. There was a similar relation between the reactions in this case.

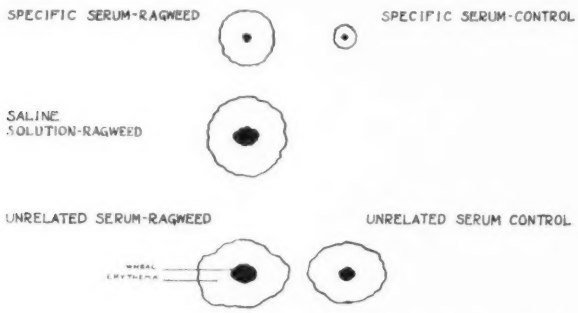

Fig. 1.—Neutralization of antigen: graphic representation of the reactions of a naturally sensitive recipient.

TABLE 2.—*Neutralization of Antigen (Tests Performed on Naturally Sensitive Skin)*

Injection, 0.01 cc., 0.0006 Mg. of Antigen Nitrogen per Cc.	Reaction Wheal, Mm.	Erythema, Mm.	Injection, 0.01 Cc., Control	Reaction Wheal, Mm.	Erythema, Mm.
Specific serum-ragweed.....	4 x 4	25 x 25	Specific serum	3 x 3	10 x 10
Saline solution-ragweed.....	12 x 8	35 x 35			
Unrelated serum-ragweed.....	11 x 8	40 x 30	Unrelated serum	7 x 6	35 x 25

The reaction to the specific serum-cod mixture approximated the size of its control. The reaction to the unrelated serum-cod mixture was notably larger than its control. The reaction to the saline solution-cod mixture and that to the unrelated serum-cod mixture were both considerably larger than that to the specific serum-cod mixture. Such results afford strong presumptive evidence of the neutralization of antigen.

The results of similar studies in which five common antigens were used (egg white, peanut, codfish, horse dander and ragweed) are summarized in table 4.

Of seventeen observations, four were discarded because the antigen concentration was not great enough to produce significant reactions in

the recipients or because the serum controls were so large as to obscure comparison. No evaluation can be made if the reaction to the saline solution-antigen mixture is not significantly larger than the serum control reaction. Twelve of the thirteen remaining experiments showed neutralization of the antigen in mixtures in which the antibody was in excess (from 1*a* to 13, table 4), as evidenced by cutaneous reactions similar to the typical examples described in tables 2 and 3 and in figures 1 and 2. In each of the twelve observations the cutaneous responses to the mixtures were similar in both subjects.

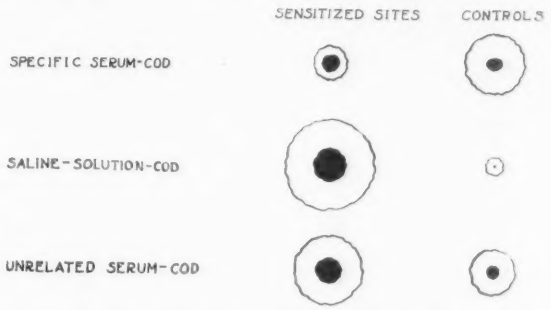

Fig. 2.—Neutralization of antigen: graphic representation of the reactions of a normal recipient with passively sensitized sites.

TABLE 3.—*Neutralization of Antigen (Tests Performed on Normal Recipient with Passively Sensitized Sites)*

Injection, 0.025 Cc., 0.003 Mg. of Antigen Nitrogen per Cc.	Reactions in Sensitized Sites		Reactions in Normal Skin (Controls)	
	Wheal, Mm.	Erythema, Mm.	Wheal, Mm.	Erythema, Mm.
Specific serum-cod	8 x 7	15	7 x 5	25
Saline solution-cod	13 x 13	40	0	8
Unrelated serum-cod	11 x 10	30	5 x 5	20

It may be noted in the table that, in general, for a given antigen, parallelism exists between the antibody titer of the serum and the amount of antigen neutralized. The correlation is not exact, for no attempt was made to determine in each case the maximal amount of antigen which could be neutralized.

In six observations, mixtures were included which contained antigen in excess of the minimal antibody concentration. Only a fraction of the antigen was neutralized. The magnitude of this fraction determined the size of the cutaneous reaction produced. If the greater part of the antigen was neutralized, the cutaneous reaction approached the serum control reaction in size. If a small fraction of the antigen was neutral-

ized, the cutaneous reaction approached in size that to the saline solution-antigen mixture. In two instances both recipients showed partial neutralization, while in one instance neither of the recipients showed evidence of neutralization.

In the remaining three of the six observations with mixtures containing antigen in excess, one of the two recipients showed partial neutralization, while the other showed none. Such differences between the two recipients may be expected in an experiment in duplicate (*6b*, *9b* and *10b*, table 4), for moderate differences in "free" antigen cannot always be demonstrated, depending in part at least on the natural reactivity of the skin tested.

Such inconstant results are in marked contrast to the consistent results obtained in the group of observations with mixtures containing an excess of antibody. In that group, neutralization of the antigen, as judged by the cutaneous reactions, regularly occurred, and the two recipients in each observation invariably gave closely comparable reactions.

TABLE 4.—*Antigen Neutralization Studies (Tabulation of Results)*

No.*	Antigen	Antibody Titer, Units†	Mg. of Antigen Nitrogen per Cc. in Test Mixture		
			Neutralization	Partial Neutralization	No Neutralization
		Antibody in Excess			
1*a*	Peanut	30+	0.0003‡		
2*a*	Peanut	30+	0.0003		
3	Peanut	600+	0.003		
4	Peanut	1500+	0.006		
5	Peanut	6000+	.....	.....	0.03
6*a*	Egg	150+	0.0006		
7	Egg	600+	0.006		
8*a*	Codfish	600+	0.003		
9*a*	Horse	300+	0.0006		
10*a*	Ragweed	60+	0.0003		
11	Ragweed	60+	0.0006		
12	Ragweed	300+	0.0015		
13	Ragweed	600+	0.006		
		Antigen in Excess			
1*b*	Peanut	30+	.....	0.0006, 0.0015‡	
2*b*	Peanut	30+	.....	0.0006, 0.0015	
6*b*	Egg	150+	.....	0.006	0.006
8*b*	Codfish	600+	.....	.....	0.03, 0.03
9*b*	Horse	300+	.....	0.03	0.03
10*b*	Ragweed	60+	.....	0.006	0.006

* The letters *a* and *b* indicate the use of weak and strong antigen mixtures, respectively, with the same serum.

† One unit of passive transfer antibody is defined as the amount of antibody neutralized by the quantity of antigen which contains 0.00001 mg. of total nitrogen per cubic centimeter. The titer can be determined only within the limits of the last reacting and the first non-reacting site of the titration series and is, therefore, expressed here as the minimum level plus a small indeterminate amount. Thus 30+ units indicates equivalence to more than 0.0003 mg. of antigen nitrogen per cubic centimeter.

‡ When the mixtures contained antibody in excess, the results in two recipients were the same. When they contained antigen in excess, differences were observed in some pairs of recipients. The results of the tests in each recipient are therefore recorded separately for the latter group.

Heat-Inactivated Serum.—Since it is well known that heating sensitizing serum at 56 C. for thirty minutes or more will markedly reduce or abolish its sensitizing power, it seemed of interest to investigate the effect of heat on the neutralizing power of such serum. For this reason, parallel observations with heated passive transfer serum were included in eight of the thirteen experiments with test mixtures of which the results have been tabulated.

The heat-inactivated serum was prepared by heating samples of the undiluted serum in a water bath at 56 C. for thirty, sixty, ninety and one hundred and twenty minutes (longer when necessary); an intracutaneous site was treated with 0.1 cc. of each sample and tested twenty-four hours later by an intramuscular injection of antigen. The first nonreacting site of the series was taken to indicate the time necessary for inactivation. Nine of the serums were inactivated at thirty, sixty or ninety minutes. Four required two hours, two hours and a half, three hours and seven hours, respectively. It is interesting that the serum requiring seven hours had the highest antibody titer of the series (6,000+ units).

For each group of tests the heat inactivated serum was mixed with antigen in the same amount and with the same final antigen nitrogen concentration as the other serum mixtures of that group, namely, specific serum-antigen and unrelated serum-antigen. The tests were performed as previously described.

In these observations, mixtures of heat-inactivated serum and antigen never produced reactions as large as those of the saline solution-antigen and unrelated serum-antigen mixtures. In ten recipients the reactions were no larger than those of the serum controls; in four the reactions were intermediate in size between the control and the saline solution-antigen and unrelated serum-antigen reactions. These results suggest that destruction of the sensitizing power by heat is not paralleled by a destruction of the neutralizing power, which is retained entirely or is only partially impaired.

Loss of Neutralizing Effect When Mixtures Are Stored.—In two instances the mixtures were stored for three weeks and the tests were then repeated. In both instances, although neutralization had been clearly demonstrated before, no neutralization was evident on the second trial.

COMMENT

The phenomenon of the neutralization of antigen by specific passive transfer antibody is of interest in connection with the general question of the similarity or lack of similarity between the mechanism of animal anaphylaxis and that of human allergy. It is well established that ana-

phylactic antibody (precipitin) neutralizes antigen in vitro so that the antigen no longer is capable of sensitizing the guinea-pig.[8]

Levine and Coca [3a] advanced the failure of the neutralization of atopen by reagin as added evidence of the differentiation of the two mechanisms. In the most recent edition of "Asthma and Hay Fever," by Coca, Walzer and Thommen,[9] the early observation of Levine and Coca on which this statement is based is quoted:

> Although the atopic excitant is capable of inhibiting the sensitizing power of the reagin, the atopic reagin may completely lack any of the property of specific inactivation of the corresponding atopen.

Jadassohn, whose earlier experiments [10] also indicated an absence of neutralization of antigen, subsequently demonstrated specific neutralization of ascaris antigen and rejected his earlier experiments with the following statement:

> From these considerations [the quantitative relationships] which I did not apply to earlier experiments, it becomes obvious that we must be very careful not to conclude, from negative results, that a neutralization of the antigen cannot take place, for there is always the possibility that it could be shown under other quantitative conditions. But we cannot always change these quantitative considerations at will.[2a]

More recently Coca stated that he had confirmed Jadassohn's findings with ascaris serum and had also "encountered a hay-fever subject who was ascaris sensitive and whose anti-pollen reagins were capable of partially inactivating the pollen excitant." [11]

Harley [2b] has also published the results of experiments on the neutralization of pollen antigen by allergic specific serums, but he has not defined the quantitative factors underlying the phenomenon.

Storm van Leeuwen and Kremer [3b] described an antigen-inhibiting effect of some human allergic serums and ascribed this action to an inhibiting substance. In a subsequent paper Kremer [3c] stated that the inhibiting substance, while often associated with the transmission substance, is not identical with it. Cooke and his co-workers [12] also sug-

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8. Doerr, R., and Moldovan, J.: Analyse des Präzipitationsphänomenon mit Hilfe der anaphylaktischen Reaktion, Ztschr. f. Immunitätsforsch. u. exper. Therap. **5**:125, 1910.

9. Coca, A. F.; Walzer, M., and Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, Publisher, 1931, p. 47.

10. Jadassohn, W., and Zarusky, M.: Idiosynkrasie gegen Sellerie, Arch. f. Dermat. u. Syph. **151**:93, 1926.

11. Coca, A. F.: A Critical Review of Investigations of Allergic Diseases, Ergebn. d. Hyg., Bakt., Immunitätsforsch. u. exper. Therap. **14**:538, 1933.

12. Cooke, R. A.; Barnard, J. H.; Hebald, S., and Stull, A.: Serological Evidence of Immunity with Coexisting Sensitization in a Type of Human Allergy (Hay Fever), J. Exper. Med. **62**:733, 1935.

gested the coexistence of sensitizing and neutralizing antibodies. Whether the sensitizing and neutralizing powers are functions of the same or of separate antibodies is perhaps still an open question.

The experimental results obtained with heat-inactivated serum indicate a partial or complete retention of neutralizing power after the sensitizing power has been destroyed. This is in accord with the experiments of Jadassohn [2a] with ascaris serum-antigen mixtures; he showed that heating the ascaris-sensitive serum for twenty-four hours did not remove its neutralizing power.

The stability of neutralized mixtures has been investigated by Jadassohn [2a] and Harley [2b] in observations on the effect of heat on such mixtures. Their results were conflicting, the former finding that the antigen-antibody combination is not dissociated by heat, and the latter, that it is. In our studies, storage of two serum-antigen mixtures in the icebox for three weeks caused the neutralizing effect of the serum on its antigen to disappear. The data do not permit conclusions as to the stability of the neutralized mixtures.

The demonstration that antigen neutralization by passive transfer antibody occurs with notable regularity when quantitative relationships are observed eliminates one of the proposed criteria of differentiation between the mechanisms of animal anaphylaxis and human allergy.

SUMMARY AND CONCLUSIONS

Studies with serum-antigen mixtures prepared with consideration of the quantitative relationship of antibody to antigen were made to determine the ability of the passive transfer antibody to neutralize its specific antigen as evidenced by the response of the naturally or artificially sensitized skin to intracutaneous injection of such mixtures.

Five common antigens were used in these observations: egg white, peanut, codfish, horse dander and ragweed.

The neutralization of antigen was demonstrated in twelve of thirteen observations on mixtures of serum and antigen prepared so as to contain an excess of passive transfer antibody, as determined by a preliminary titration.

Partial neutralization of the antigen was demonstrated in some instances but not in others with mixtures of serum and antigen prepared so as to contain an excess of antigen.

The quantitative relationships necessary for the demonstration of neutralization are discussed.

Inactivation by heat of the sensitizing power of the passive transfer antibody is not necessarily paralleled by a diminution in its neutralizing power.

Case Reports

ALBINISM

ALBINISM AND UNIALBINISM IN TWIN AFRICAN NEGROES

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Since only 2 authenticated cases of albinism in 1 of twins have ever been reported, the condition is of sufficient interest, I believe, to warrant the report of a third case.

Albinism, known also as congenital leukoderma, congenital achromia and congenital leukasmus, is a congenital absence of pigment in the skin, hair and eyes.

It is definitely hereditary and familial. Under the mendelian theory of heredity it is considered a recessive characteristic. For the sake of clarity it might be well to review briefly the work carried out by Abbé Gregor Mendel in 1865 and his theory deduced therefrom. He studied the effect of crossing different varieties of peas and evolved a law of heredity. Though similar experiments cannot be carried out with man, a careful analysis of pedigrees indicates that the same law holds good. Mendel took different varieties of the edible pea, one tall and the other short, and crossed them. All the cross-bred seeds grew into tall plants, closely approximating the tall variety. Because the character of tallness appeared in the cross-bred plant to the exclusion of the opposite character, he termed it a dominant character, and the tendency to dwarfism he called recessive. In the first generation, hybrids preserve the peculiarity of one or the other parent and do not exhibit a blend of the peculiarities of the two. When these hybrids interbreed the recessive character makes its appearance in one fourth and the dominant character in three fourths of the descendants. It was found that when plants having the recessive character were united all the offspring were marked by that character. Dominant character may be recognized from the fact that it is transmitted through affected persons only. One person affected by the dominant character and one normal person produce offspring of whom about 50 per cent are affected.

That albinism is a recessive character is shown by the fact that it may appear in the children of parents who are not albinos and is especially likely to occur in children born of consanguineous marriages, particularly when the marriage is one of first cousins.

From l'Hôpital de Sakbayemé.

Magnus [1] found that the 108 cases of albinism in Norway in which he had information regarding heredity occurred in a total of 50 families. In his compilation the albinism showed a recessive mendelian character in some instances and a dominant character in others. In 13 marriages between cousins, there were 27 albinos among the offspring and 69 normally pigmented children. In 2 marriages between uncle and niece, 2 of the 9 children were albinos. In 6 marriages between less close relations, 14 of the 23 children were albinos, and in 35 nonconsanguineous marriages there were 62 albinos to 96 normally pigmented children.

Some persons believe that albinos were once a separate race and that the condition is atavistic; others believe that it is a disease or the result of disease. Lecat attributed it to the influence of heat; Mansfield and others, to maternal impression. The last-mentioned theory is prevalent in the Philippines,[2] as is the theory that the condition is due to the morbid imagination of the mother during gestation. The consensus seems to be that the condition is due to faulty development of the pigment-producing apparatus. Just what causes this is not known, but, as suggested by Niles, Musser [3] and others, it may be a metabolic disturbance in which the pigment of the body is not so prepared that it may be utilized in the skin, eyes and hair.

The belief held by the Basa tribe, in the French Cameroun, is that the mother conceives the albino by a water spirit, and to break the spell so that no more albinos will be born the husband goes into seclusion for nine days in a shelter built by his own hands beside the nearest river. Food is brought to him at night, but he must see no one and speak to no one. There is also a belief that if the mother stoops to walk under or places her hand on the food drier which hangs over the fire, the albino child will die. Since it is impossible for a housewife to carry on her daily routine without doing either one or both of these things, that the desire is parent of the superstition is obvious. In this tribe albinos are probably born as frequently as in other African tribes, but they are only rarely permitted to survive, so keenly are they held in disrepute.

The Bulu people, a large neighboring tribe, believe that the birth of an albino comes as a result of adultery or other sin of one or both parents and that when an albino is sitting with his legs across the path of a pregnant woman if she steps over them instead of walking around her child will be an albino. The latter belief, however, applies not only

1. Magnus, V.: Albinism in Man, Norsk mag. f. lægevidensk. **83**:509, 1922; abstr., J. A. M. A. **79**:780 (Aug. 26) 1922.

2. Knowles, F. C.: Family Albinism, Interstate M. J. **23**:555 (July) 1916.

3. Musser, J. H., Jr.: Albinism in Negro, M. Clin. North America **8**:781 (Nov.) 1924.

to albinism but to any physical or mental abnormality of the person stepped over. In this tribe the albino offspring are cared for as well as the normal children in the family, but their birth is nevertheless regarded as a calamity. Regardless of the superstitions concerning albinos, the belief that heredity is the biggest single factor is held to strongly by all tribes.

The exact frequency of albinism is not known, but it is more common in some races than in others. The Negro races are more prone to the condition than the white. The so-called white Indians of Mexico and South America are supposed to have been a race of albinos. Magnus [1] succeeded in obtaining the records of 174 albinos in Norway. The proportion to the general population was 1 to 9,649.

Sutton [4] suggested that although albinism is apparently endemic in certain tropical countries (such as Lower Guinea), its comparatively frequent occurrence in these regions is possibly a result of consanguinity. This, however, cannot be a causative factor in tropical Africa, since there has always been, for eugenic or other reasons, an unwritten intertribal law that persons to be married must come from entirely different clans, usually fairly remote from each other. As a result, the African husband and wife are not even distantly related, except in rare instances, in which the fact is unknown to the families involved.

According to G. Saint-Hilaire, albinism occurs more frequently in females than in males. The reverse is true in my field of observation. Whether more male than female albinos are permitted to live, a question impossible for a white man to answer, is not known, but in traveling through the villages one sees 2 or 3 male albinos to every female albino.

Burton, as cited by Knowles,[2] wrote that in West Africa a condition is occasionally observed which might be termed semialbinism, in which the skin varies between the natural hue of the Negroes and that of white people. This is true. This condition occurs as often as does true albinism. As to texture of the skin, and general appearance, the subjects resemble mulattos more closely than they do albinos, but the hair is negroid even though brown and the skin has more of a reddish cast. The irises are usually pale buff (a shade not seen in the white race at all) or definitely blue. There is no photophobia or nystagmus. Physically and intellectually they are the equals of their blacker brothers. The natives themselves hold the belief, which is probably well founded though no cases are known to me personally, that offspring of semialbinos are likely to be true albinos.

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4. Sutton, R. L.: Diseases of the Skin, ed. 5, St. Louis, C. V. Mosby Company, 1923, p. 549.

Knowles [2] wrote that families in which there is albinism have apparently had a large number of offspring and suggested that this may be explained by the fact that the Negro races are more commonly affected and that they normally have large families.

It may be an exaggeration to say that all albino Negroes look alike, but like mongolian idiots they have great similarity in general appearance. The facial characteristics are naturally not different from those of normally pigmented Negroes except for the constant facial distortion which results from an attempt to protect the eyes from light. The eyes are watery, blinking is frequent and without exception there is marked nystagmus. The pupils appear red and the iris pink or even bluish from reflected light. The hair differs from the normal in color only, and is a peculiar dull, yellowish white. The skin is pinkish white and is dotted with small areas of pigment similar to freckles. The skin does not tan but burns and desquamates repeatedly whenever unduly exposed to the sun's rays. While histologically the skin seems to present no pathologic changes except the absence of pigment, clinically it is certainly abnormal. It is less oily than that of normal persons, and the dryness is more noticeable in adults. More exertion is necessary to produce sweating, and then the sweating is meager. In children especially, itching lesions are constantly appearing on the skin (scabies), with small or large ulcerations. The skin is less resistant to pyogenic organisms, and more or less infection occurs with every superficial abrasion. In adults, maculopapules are usually present across the shoulders and back; these are due perhaps to irritation from the sun. In young adults the skin takes on an atrophic, crêpelike appearance and looks and feels like the skin of persons with the macular type of leprosy.

Most albinos are mentally and physically below par. The women menstruate late, although menses normally begin early in the tropics. The mental difference is probably due largely to the psychologic effect of the albino's being regarded as inferior and ridiculous from the time he is born and to his difficulty in using his eyes for gaining knowledge. J. Bulla Mfum, for twenty-one years the head native medical assistant at the Central Hospital of Elat, made the statement that in all his experience he had seen just one albino who was a "real person"; the one was an intelligent and respected man who held the position of chief of his clan.

REPORT OF A CASE OF ALBINO TWINS

For four years a normal Bulu mother and father and their 7 children were under my observation. Of the children, 5 (71.4 per cent) were albinos and 2 (28.6 per cent) were normally pigmented (fig. 1). Three of the 5 albinos were boys, and the remaining 2 were twin girls.

The first-born child, a boy albino, died in 1931 at the age of 5½ years of severe gastric symptoms of eleven hours' duration. According to the account given by the parents, the attack may have been due to intentional poisoning by a well meaning friend or relative of the family.

No albinism was known in the family of either parent. However, the mother of the maternal grandmother of the children came from a clan, the Esa la'an of the Bulu tribe, in which the percentage of albinism in the entire population is relatively high. At the time of his marriage, in December 1924, the father made the statement that if he had any albino children he would do away with them. It has definitely been proved that this was idle talk, voicing the general attitude of all natives to albino offspring, rather than a statement arising from an apprehension based on his knowledge of their family histories.

Fig. 1.—Albino twins (on the arms of the chair), with their family. The marked photophobia of the albinos is apparent even though the photograph was taken under an overcast sky in the late afternoon.

A summary of the data on this family is as follows:

Name	Sex	Age or Date of Birth	Condition
Husband—Meye me Nkpwele.....	.....	About 35 years	Normal; living and well
Wife—Okon Abeng.....	.....	About 27 years	Normal; living and well
Children			
1. Afou'ou Meye.....	Male	May 5, 1926	Albino; died, 1931
2. Nkpwele Meye.....	Male	Aug. 2, 1928	Albino; living and well
3. Nseme Meye.....	Male	May 16, 1930	Normal; living and well
4. Bindula Meye.....	Male	July 20, 1932	Albino; living and well
5. Atyam Meye.....	Female	Feb. 18, 1934	Albino; living and well
6. Nkpwe'e Meye.....	Female	Feb. 18, 1934	Albino; living and well
7. Afu'u Meye.....	Male	Aug. 9, 1936	Normal; living and well

As will be noted, the fifth pregnancy resulted in albino twins; they were identical twins. This is the only case of albino twins in this

country known to me. Hyde [5] referred to twin albinos, children of Irish parents, treated in his clinic. There were twin albinos, also, in the family of the Catalina Island twins, whose history is reviewed somewhat later in this paper.

Only two cases have been reported of albinism in one of twins, a condition which for want of a better term may be called unialbinism. When both parents carry a gene for albinism there is one chance in four that a given child will be an albino. The same law of chance, according to Windle,[6] rather than an inherent probability that one albino and one normal child will be born if albino genes are present in both parents, applies in the case of nonidentical twins.

Fig. 2.—The boy and girl, American Negroes, who presented the first known case of unialbinism in twins. The photograph was taken in 1868. (From the *Pathfinder,* July 29, 1933.)

At a medical meeting held in Leeward Islands in 1892, A P. Boon presented 2 albino Negroes, and the father related that his uncle's wife always bore twins of which one was white and the other black. If this statement could be accepted, more than two cases would be known.

The first authentic case of unialbinism was in American Negro twins who were born to normal parents about 1860 (fig. 2). One, a girl, was an albino and

5. Hyde, J. N.: Diseases of the Skin, ed. 8, Philadelphia, Lea & Febiger, 1909, p. 540.

6. Windle, E.: Three Generations of Albinism and Twinning, J. Hered. **26:** 23 (Jan.) 1935.

the other, a boy, normally pigmented. They were exhibited in 1868 at Burnell's Museum in Pittsburgh.

The second case was that of L. R. and D. R. (fig. 3), twin boys born to normal Mexican parents on the Santa Catalina Islands in 1931 or 1932. According to Dr. D. G. Bussey, of the Catalina Hospital, who delivered them, the parents were in excellent health. Windle [6] reported that the twins' grandmother's great grandmother was an albino. She married a nonalbino and became the mother of 5 boys and 5 girls. One of these girls is said to have had one-half white hair and

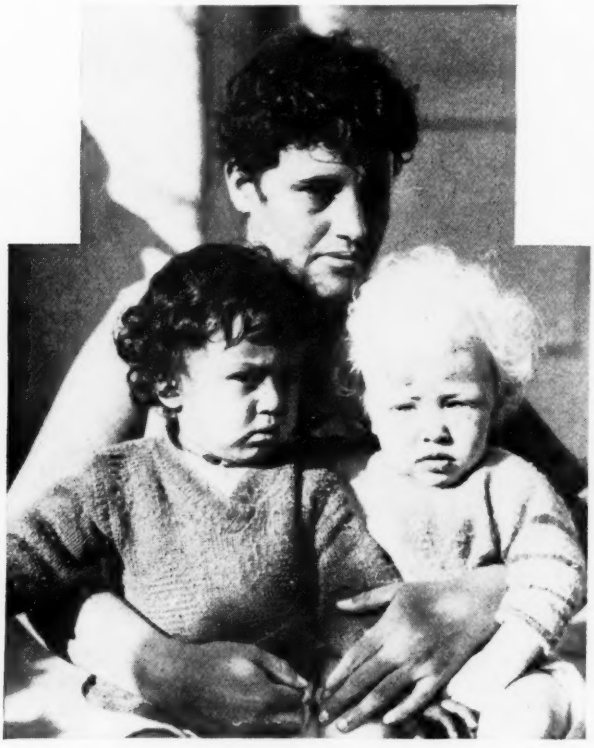

Fig. 3.—The Mexican boys who presented the second case of unialbinism in twins. They were born on the Santa Catalina Islands about five years ago. The photograph was taken in 1933.

one-half black and one blue eye and one black eye. If this story could be verified, the girl would represent one of the few cases on record of a human mosaic. A brother in the same family had one-half white hair and one-half black hair and normal eyes.

These twins' grandmother's aunt was not an albino but had 4 albino boys, among them 1 set of twins. Another aunt not an albino had 3 albino children. The albino twin was the first albino to appear in the third generation. In this family there were 3 other normal children.

REPORT OF A CASE OF UNIALBINISM

Twins, Mvom and Ntyam Mvé (fig. 4), were born to African Negro parents of the Bulu tribe at Ebolowa, French Cameroun, on Oct. 14, 1932. The albino was a boy and the normally pigmented twin a girl. The parents were normal except for having had syphilis, which was passed on to the twins. The children were seen by me only once, at the age of 7 months, on May 17, 1933. An attempt was made to keep in contact with the family for at least one course of anti-syphilitic treatment, but when the mother was told that the syphilis and the malnutrition of the twins could not be rectified in two or three days she returned with them to the forest to try native medicine.

A serious attempt was made to elicit a history from the mother for her family and that of her husband. She was positive in her assertion that to her knowledge

Fig. 4.—The boy (albino) and girl (normal) who presented the third case of unialbinism in twins, reported in this paper. They were African Negroes of the west coast, born Oct. 14, 1932, in the French Cameroun. They were photographed at the age of 7 months.

and to that of her husband there had never been albinism in the family of her husband. In her family there had been only 1 albino, an uncle of her mother. Neither parent of the twins came from the Esa La'an clan of albinos previously mentioned. There were 4 other children in the family, all of whom were normally pigmented.

It is a coincidence, but nevertheless interesting, that the 3 cases of unialbinism were different as to sex. In the first case and in the third case (the new case) both sexes were represented but the colors were reversed, and in the second case the twins were both boys.

SUMMARY

Among the members of the Basa and the Bulu tribe of the French Cameroun several superstitions exist regarding the occurrence of albinism, but in spite of this fact the people are all convinced that the condition is definitely hereditary.

Since albinism appears especially among children born of consanguineous marriages, the incidence would probably be even greater in Africa were it not for the fact that relatives, no matter how distant, are not permitted to marry.

The skin of the albino in Africa is a constant source of trouble, being constantly covered with scabies, pyogenic infections of various types or ulcerations, in addition to being in a state of chronic sunburn.

A condition of semialbinism is found in West Africa; the offspring of affected persons, according to the natives, are more than likely to be true albinos.

A case of albino twins in a family of 7 children, among whom were 5 albinos, is reported. The parents and 2 of the children were normally pigmented.

The only 2 cases previously known of unialbinism in twins are briefly reviewed. One occurred in Negro twins in the last century and the other recently in Mexican twins.

A new case of unialbinism in twins is reported. It occurred in a Bulu family in which the parents and the 4 other children were normally pigmented.

HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY IN INFANTS AND IN CHILDREN

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In pediatric literature little emphasis has been placed on the fact that clubbed fingers and toes may be but one manifestation of the condition which has been designated as hypertrophic pulmonary osteo-arthropathy, or Marie-Bamberger's [1] disease. The reason for this lack of emphasis is obvious. Clubbed fingers are found in young patients with relative frequency, but concomitant changes in other parts of the skeleton are infrequently found.

That the condition does occasionally occur in a young person is attested by the reports of Bamberger,[1b] Whitman,[2] Taylor,[3] Gilbert and Fournier,[4] Gillett (quoted by Miller [5]), Davis,[6] Hyman and Herrick,[7] Bryan [8] and Schippers.[9] As Locke [10] emphasized, the changes in the

From the Section on Pediatrics, the Mayo Clinic.

1. (*a*) Marie, Pierre: De l'ostéo-arthropathie hyperthrophiante pneumique, Rev. de méd., Paris **10**:1-36 (Jan.) 1890. (*b*) Bamberger, E.: Ueber Knochenveränderungen bei chronischen Lungen- und Herzkrankheiten, Ztschr. f. klin. Med. **18**:193-217, 1891.

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4. Gilbert, A., and Fournier, L.: La cirrhose hypertrophique avec ictère chez les enfants, Compt. rend. Soc. de biol. **47**:419-420, 1895.

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6. Davis, N. S., Jr.: Pulmonary Hypertrophic Osteo-Arthropathy, J. A. M. A. **24**:845-848 (June 1) 1895.

7. Hyman, C. H., and Herrick, T. P.: Chronic Osteo-Arthropathy: Report of a Case in a Child Aged Twenty-Eight Months, J. A. M. A. **78**:1043-1045 (April 8) 1922.

8. Bryan, Lloyd: Secondary Hypertrophic Osteoarthropathy Following Metastatic Sarcoma of the Lung: Report of a Case, California & West. Med. **23**:449-452 (April) 1925.

9. Schippers, J. C.: Eine seltene Komplikation bei Bronchopneumonie (sog. ostéoarthropathie hypertrophiante pneumique), Monatschr. f. Kinderh. **45**:130-140, 1929.

10. Locke, E. A.: Secondary Hypertrophic Osteo-Arthropathy and Its Relation to Simple Club-Fingers, Arch. Int. Med. **15**:659-713 (May) 1915.

digits and the skeleton are nearly always secondary to some primary disease of the lungs, heart, liver or other organ or part of the body, suppurative pulmonary disease being responsible for the changes in most of the cases. In the cases reported by these authors, in which the condition affected children, the primary lesions included congenital heart disease, pneumonia and cirrhosis of the liver, as well as bronchiectasis and empyema.

Locke stated that clubbing of the fingers secondary to various conditions frequently appears quickly but that osteo-arthropathy seldom develops earlier than at least three or four years after the appearance of the pulmonary disease. This may be one reason why osteo-arthropathy is seldom observed in infants. Another probable reason is that although changes in the skeleton occur in conjunction with clubbed fingers in a considerable proportion of the cases, the changes have not progressed to the point of causing symptoms; hence, the skeleton does not receive close study.

It is generally conceded that in clubbed fingers the changes are almost always limited to the soft tissue. There are on record, however, cases in children as well as in adults in which an irregular, burlike widening of the distal phalanges has been observed roentgenographically. The question as to different types of clubbing caused by various diseases has been answered by many writers with the statement that no essential differences exist. The rate of development may cause some difference in the appearance of the digits. According to Locke, clubbing that develops rapidly, as in empyema, exhibits extreme swelling, deep injection and swelling of the nail beds and redness of the nails, but in the more slowly developing type there are less swelling, little if any injection of the nail beds and, frequently, cyanotic nails.

Locke stated further that in the rest of the skeleton the changes consist of slowly progressive ossifying periostitis, beginning usually in the distal ends of the diaphyses of the bones of the forearms and the legs and later involving also the other bones of the limbs and even in some cases nearly all the remaining bones of the skeleton. Later in the course of the disease, and coincident with the periosteal proliferation, there is also rarefying osteitis of the shafts, with fatty changes in the marrow. At first the new periosteal bone is clearly differentiated from the old, but later (two or three years afterward) the two become more or less fused and in most places are indistinguishable. The joints may show swelling and erosion of the cartilage, and they are sometimes involved in a destructive process. The changes in the bones may undergo periods of regression and exacerbation according to fluctuations in the severity of the primary disease and, as illustrated by Schippers' case of a child aged 2½ years and by Bryan's case of a boy aged 12, they may disappear entirely if the primary disease clears up completely.

The nature of the process or processes which account for clubbing of the digits and changes in the skeleton is not known. A number of explanations has been offered. Marie and Bamberger held that the changes were due to toxins absorbed from the region primarily diseased. Others hold that the changes are caused by anoxemia. Janeway [11] stated that perhaps stasis in the peripheral parts of the body caused a concentration of toxic products at those parts, thus favoring periosteal reaction. Because of the frequency with which the changes are observed in adults with pulmonary tuberculosis and because of the character of the newly formed periosteal tissue, some investigators contend that the entire picture is based on tuberculous infection and intoxication. In five of the cases collected by Locke no primary disease was demonstrable, and hence it appears that occasionally the condition may develop independently. However, the overwhelming evidence furnished by the cases on record suggests that in them the condition was not independent but was secondary to some obscure lesion or lesions.

A brief review of the cases reported of hypertrophic pulmonary osteo-arthropathy in children may be of interest. Since the cases in which there was clubbing of the digits only are not of special interest in this connection, they are not described.

Bamberger included in his report the case of a boy aged 7 years who had been cyanotic since birth. No other detail of the history was obtainable. This boy died from congenital heart disease, with heart failure, and the periosteum of the lower half of both tibias was found to be reddened, somewhat thickened and easily detachable. Under it the bones, particularly the external surfaces, were covered by a delicate red tissue. On the upper halves of the tibias as well as on the femurs and the bones of the forearm the periosteum was pale, thin and firmly attached. Whitman's patient was a girl aged 5 years. At the age of 2 years Pott's disease developed, and at the age of 3 she had pertussis, which left her with a persistent productive cough. At the age of 4½ clubbing of the fingers was noted by her parents, and at 5 her knees and ankles became swollen and the bones of her forearms became enlarged and tender. Roentgenograms revealed changes in the metacarpal and the phalangeal bones.

Taylor in 1895 published a paper on cirrhosis of the liver in childhood. In it he referred briefly to three cases, the patients being 6, 12 and 13 years old, respectively, in which there was widening of the distal phalanges and of the extremities. Gilbert and Fournier published a paper in 1895 on cirrhosis of the liver with icterus in childhood. In two cases, in which the disease had begun at the age of 5 and of 4

11. Janeway, T. C.: Hypertrophic Osteoarthropathy, with Report of Two Cases, Am. J. M. Sc. **126**:563-581 (Oct.) 1903.

years, respectively, there were clubbing and some deformity of the extremities.

Gillett saw a patient with typical hypertrophic pulmonary osteo-arthropathy, a boy aged 12 years who had had repeated attacks of bronchitis since the age of 4 years. Davis reported the case of a boy aged 4½ years who had had pneumonia at the age of 1 year. This was followed by a persistent cough and expectoration of large amounts of purulent sputum. At the age of 2 his parents had noted clubbing of his fingers and toes and enlargement of his wrists and ankles. The diagnosis was empyema with bronchial fistula and hypertrophic pulmonary osteo-arthropathy. Hyman and Herrick reported the case of a girl aged 28 months. Attention was first directed to her clubbed fingers when she was brought to a physician for treatment of a burn. Examination revealed marked thickening of all the long bones, clubbing of the toes as well as of the fingers, burlike widening of the distal phalanges and congenital enlargement of the heart.

Bryan, in a paper dealing with osteo-arthropathy in a case of sarcoma of the lung, mentioned a second case, that of a boy aged 12 years who had empyema and osteo-arthropathy, the latter clearing up after successful surgical treatment of the empyema.

Schippers observed a girl who had had pneumonia at the age of 2 years. Resolution of the pneumonia was delayed, and after four months her hands became swollen. Roentgenograms made two weeks after the appearance of the swelling showed periostitis of the second, third and fourth metacarpal bones of the right hand and of the third and fourth metacarpal bones of the left hand. The swelling gradually subsided as her temperature became normal and as the pulmonary condition cleared up. Roentgenograms made one year after the swelling had first been noted revealed that the periostitis was no longer present.

This group of cases of hypertrophic pulmonary osteo-arthropathy in children seems surprisingly small when compared with the number of cases of clubbed digits that may be encountered by clinicians and when compared with the incidence of osteo-arthropathy among adults. No doubt more intensive study, especially by roentgenographic methods, of children with clubbed digits would reveal additional instances of osteo-arthropathy. The group is sufficiently large, however, to indicate that the condition does occur in young persons and that the primary disease may involve the lungs, the heart or the liver.

REPORT OF A CASE

To this group I should like to add another case which is of especial interest because the patient was very young, younger in fact than any of those of whom record has been found. He was a boy aged 7½ months. He was brought to the clinic because of restlessness and heavy breathing, which had been present since

he was 3 weeks of age. Four grandparents, his father, mother and one sister, aged 2½ years, were living and well. The patient had been born by cesarean section, and the weight at birth was 7 pounds (3,175 Gm.). Respiration after birth had begun spontaneously.

This child was ill almost constantly from the age of 3 weeks until his death. At the age of 3 weeks pyoderma developed, with cutaneous lesions which were pustular and pemphigoid. At about the same time there appeared what was thought to be cellulitis around the umbilicus, inflammation of the entire abdominal wall and enlargement of the superficial veins which lead away from the umbilical region. This subsided. At the age of 1 month purulent dacryocystitis developed on the right side; two weeks later there was inflammation of the inguinal lymph nodes. At the age of 8 weeks the child had an infection of the upper part of the respiratory tract, with marked cervical adenitis. The cervical lymph nodes on one side suppurated and were incised and drained. At the age of 10 weeks, 10 cc. of convalescent scarlet fever serum was administered in an effort to overcome the infection.

A fresh infection of the upper part of the respiratory tract then developed, and this failed to clear up. At the age of 4 months, dyspnea developed, which lasted about two days. At that time examination of the thorax revealed impaired resonance and tubular breath sounds on the right, and a roentgenogram revealed increased density of nearly the entire right side of the chest, the cardiac angle and the diaphragmatic angles being obliterated. Thoracentesis was performed, and 5 cc. of pale yellow fluid was obtained, the fluid coagulating almost immediately after being withdrawn. After one week the infant appeared to be nearly normal, but some dulness persisted over the right side of the thorax.

At the age of 5 months the child again acted as if he were unwell. His spleen and liver were found to be enlarged. The percussion note on the right side of the thorax was dull; the breath sounds were only slightly reduced on that side. Examination of the blood at this time revealed moderate hypochromic anemia. A differential blood count showed 2 per cent myelocytes and 23.5 per cent monocytes. Examination of the blood a month later disclosed essentially the same picture. At the age of 6 months and again at 7¼ months the patient received transfusions of blood.

At the time of the child's admission to the clinic, at the age of 7½ months, his color was fairly good but his respiration was rather labored. He appeared to have a mild infection of the upper part of the respiratory tract. Percussion of the right side of the thorax yielded a dull note, and the breath sounds over this area were tubular. The heart appeared to be normal. The spleen was moderately enlarged. There was marked clubbing of the digits (fig. 1).

A roentgenogram of the thorax (fig. 2) showed an almost homogeneous increase in density, which involved the upper two thirds of the right thoracic area and had a rather sharply defined and somewhat rounded lower border. The heart and the trachea were displaced to the left, as though by a tumor. The diagnosis of the pulmonary condition was uncertain, but because of the history of repeated infections and because of a lighter spot in the center of the dull area as seen in the roentgenogram, a diagnosis of inflammatory exudate was favored. Thoracentesis yielded no fluid. Radium was applied over the affected part of the lung, and a roentgenogram two days later showed no change. A roentgenogram made nine days later (fig. 3) showed a slight reduction in the extent and some reduction in the density of the central portion of the shadow. The breath sounds were found to be no longer tubular.

Repeated examinations of the blood revealed moderate anemia, leukopenia and lymphocytosis and marked monocytosis. The monocytes increased to as high as 62

Fig. 1.—Photograph of the patient's hands, showing clubbing of the fingers. The darker color of the finger tips and nails is apparent.

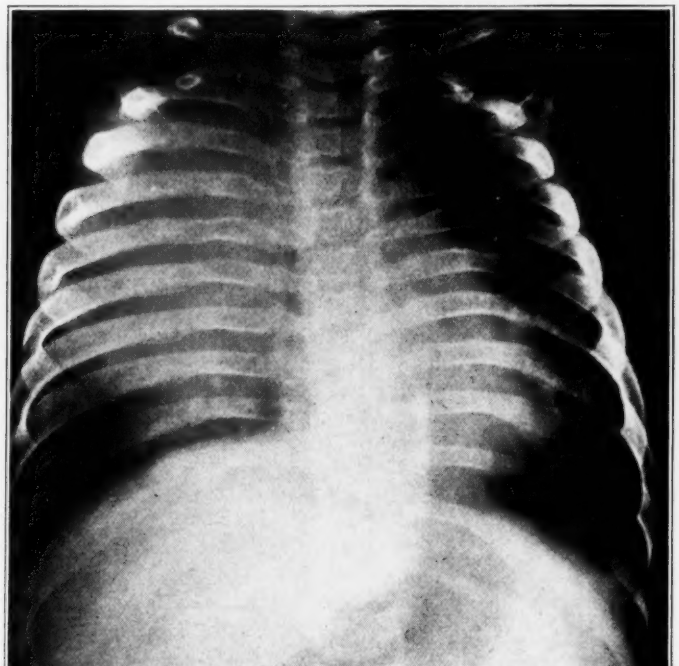

Fig. 2.—Roentgenogram of the thorax made a short time after the patient was admitted to the hospital. The area of homogeneous increased density involves all but a portion of the lower part of the right thoracic cavity. The shadows of the ribs are abnormally wide as a result of diffuse periosteal proliferation.

per cent of the total number of leukocytes. Eosinophilic leukocytes numbered as high as 20 per cent. The few neutrophilic polymorphonuclear leukocytes present showed changes which were described as indicating a very toxic state. Study of the capillaries in the fingers showed long loops, both limbs of which were equal in caliber—changes typical of clubbed fingers. Urinalysis revealed the presence of albumin in moderate amount, bile and, on one occasion, casts. The flocculation test for syphilis and the intradermal tuberculin tests gave negative results.

Roentgenograms of the skeleton revealed diffuse laminated thickening of all the long bones. The ribs were diffusely widened and increased in size, as were

Fig. 3.—Roentgenogram made nine days after the one reproduced in figure 2, showing the reduction in size and in density of the homogeneous shadow.

the metacarpal bones and the phalanges. The cortex was thin, especially the metaphysial portion, and the internal structure of the long bones exhibited a rather homogeneous ground glass appearance. The epiphyses were normal (figs. 4, 5 and 6).

Two weeks after the patient's admission to the hospital, rib resection was carried out. The pleura was found to be greatly thickened. A multilocular pocket was encountered, and it was not possible to determine whether this was in the lung or between the lobes. About 5 cc. of pus was evacuated. After the operation the child did not do well. Eight transfusions of blood were given at intervals of four or five days. Leukopenia persisted, the leukocytes numbering 1,500 per cubic millimeter. Ten days after the operation jaundice appeared, and shortly afterward

Fig. 4.—Roentgenogram of the patient's hand, showing that the metacarpal bones and the phalanges are somewhat wider than normal. There is no burlike widening of the distal phalanges. The widening of the shadow of the soft tissues about the terminal phalanges is well shown.

Fig. 5.—Roentgenogram of the patient's arm, showing the thin cortex in the extremities of the diaphyses and the diffuse laminated thickening of the periosteum of the humerus, radius and ulna.

duodenal drainage by means of a tube was instituted. Furunculosis and suppurative otitis media then developed. The child went steadily downhill and died six weeks after admission.

The significant changes observed at necropsy were in the lungs and the bones. Scattered throughout the upper and middle lobes of the right lung were abscesses which measured up to 3 cm. in diameter. The pleura covering the affected portions of the lung was greatly thickened. There were a few small abscesses in the left

Fig. 6.—Roentgenogram of the patient's legs, showing the thin cortex and rather homogeneous ground glass appearance of the bones and the laminated thickening of the periosteum.

upper lobe. Microscopic examination of the right lung revealed bronchopneumonia in addition to the abscesses. On gross examination of the ribs and the femurs no definite change could be seen in the periosteum. On microscopic examination, however, the periosteum was observed to be greatly thickened, fibrosed and hyalinized (fig. 7). There was no evidence of inflammation other than an occasional lymphocyte.

In view of the roentgenographic and pathologic changes observed in the skeleton in this case there appears to be no doubt that it was one of osteo-arthropathy secondary to suppurative pulmonary disease. The questions which naturally arise are: 1. What was the connection between the pulmonary disease and the skeletal changes? 2. Why are skeletal changes not observed more frequently in children with similar types of pulmonary involvement?

There is no adequate reply to these questions. As indicated in the forepart of this paper, the cause of the skeletal changes is a matter of speculation. The view that they were due in this case to the action

Fig. 7.—Photomicrograph of a portion of periosteum from the femur. At the upper border, remnants of the cellular portion of the periosteum can be seen as frayed tissue. Immediately contiguous is the thickened, hyalinized periosteum, which was estimated to be from twenty to one hundred times as thick as normal periosteum. This hypertrophic periosteum merges into the skeletal muscle. There is no definite evidence of inflammation.

of toxins derived from the site of the primary lesion is supported by the almost complete absence of evidence of inflammation in the thickened periosteum. On the other hand, none of the data, historical or clinical, explained why this particular patient should be so affected while other patients with similar pulmonary disease exhibit no such changes. It appears logical that the infrequency with which the condition is seen may be partially accounted for by the assumption that a special pre-

disposition on the part of the person is necessary (an assumption which has already been expressed).

It is evident from this case that skeletal changes can develop in a relatively short time, a much shorter time, in fact, than that which has been thought necessary. The extreme youth of the patient can hardly be considered the factor which accounts for the change, since other instances of hypertrophic pulmonary osteo-arthropathy in patients less than 1 year of age have not been reported.

SUMMARY

Hypertrophic pulmonary osteo-arthropathy, or Marie-Bamberger's disease, in children has been reported infrequently. The chief features of the disease are diffuse periosteal proliferation and the formation of new periosteal bone on the shafts of the long bones in conjunction with clubbing of the digits. The condition is almost always secondary to cardiac, hepatic or, more frequently, pulmonary disease.

In the case reported in detail here, the relationship between clubbed fingers and changes in other parts of the skeleton is emphasized, and the case illustrates the fact that the changes in the long bones can develop in a period of months rather than of years and hence can occur in the first half-year of life. This suggests that when clubbed fingers are found in infants and in children, roentgenographic study of the skeleton should be carried out and may reveal the presence of pulmonary osteo-arthropathy.

Progress in Pediatrics

OSTEODYSTROPHIA FIBROSA

REPORT OF A CASE IN WHICH THE CONDITION WAS COMBINED WITH PRECOCIOUS PUBERTY, PATHOLOGIC PIGMENTATION OF THE SKIN AND HYPERTHYROIDISM, WITH A REVIEW OF THE LITERATURE

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The child whose history is recounted in the following pages exhibits a syndrome of developmental anomalies which has few counterparts in recorded medical experience. She has been a patient of the Babies Hospital for the past five years. Although the diagnostic investigations which have been carried out during this period have yielded informative results, the basic problems in normal and pathologic physiology which the child presents remain unsolved. Justification for selecting the present time to publish the record derives from the recent acquisition of information concerning a small number of patients with an identical or similar condition and from a desire to stimulate the publishing of reports of like cases which have doubtless come to the attention of physicians but which have remained unrecorded.

REPORT OF CASE

History.—The patient, a white girl, was born in New York on Sept. 9, 1926. The parents were Jews. The mother, a woman of Russian descent, was 19 years old; the father, whose forebears came from Hungary, was 22 years of age. Both parents were healthy, and they were not related by blood. The patient was their first child; a boy who was born seven years later is now 3 years old and is physically sound. The mother has had no abortive pregnancies. The patient was born at term by normal spontaneous delivery, after moderately severe labor, which lasted twenty-four hours. Her condition at birth is said to have been good; she weighed 3,410 Gm. (7 pounds and 8 ounces).

Information concerning the health of the infant during the neonatal period is scanty and indefinite. During the first few days of life she became deeply jaundiced; the intensity and duration of the icterus were such as to lead to a diagnosis of congenital atresia of the bile ducts. However, after an indeterminate period the jaundice faded; the time at which it disappeared is not known. Aside

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from this episode the first eighteen months of the patient's life passed uneventfully. Artificial feeding was instituted shortly after birth. Orange juice and cereal were added to the diet when the patient was 3 months old, vegetables when she was 7 months old and eggs when she was 12 months old. Cod liver oil was not given until the end of the first year. Although the infant regurgitated her feedings consistently during the first year of life, the appetite remained good and the evacuations regular. She sat alone at the age of 7 months and cut her first tooth at about the same time. It is asserted that she commenced to talk before she was 1 year old. She began to walk at 14 months. She probably grew in length and gained weight normally, although exact measurements were not preserved.

The parents noted nothing unusual about the infant's skin from the time the jaundice subsided until she was 2 years of age, when they "suddenly" became aware of the presence of numerous irregularly shaped patches of brownish pigmentation. Precisely when these appeared and how they developed we have not been able to ascertain. They probably have undergone no noteworthy change since the girl was 2 years old.

At the age of 2 years, without warning, the child commenced to menstruate irregularly. Simultaneously, the breasts began to enlarge and a sparse growth of axillary and pubic hair made its appearance. These features developed progressively during the ensuing months, with the result that the child appeared sexually mature by the time she was 4 years old. So far as can be determined, the evolution of her mentality and of her emotional outlook did not keep pace with her physical development but remained more closely related to her chronological age. Psychometric examination in the Neurological Institute of New York when she was 4 years old showed that her intelligence quotient was 1.13, indicating only slightly greater than average mental attainment.

The occurrence of the pigmentary phenomena and the onset of physical maturity at the age of 2 years drew the attention of the parents to a manifestation which they had noted when the infant was scarcely more than 1 year of age but to which they had paid little attention, namely, that the legs were becoming progressively bowed. This deformity developed insidiously. Although the child had begun to walk at the age of 14 months, at 2 years her lower extremities had become so curved that locomotion was difficult. When she was 3 years of age bilateral osteotomy was performed, in the New York Orthopaedic Hospital, because of coxa vara and knock knee on the right side and bowleg on the left side. Specimens were not obtained for microscopic examination. The bones healed promptly after operation. Several months later, when the child was 3 years and 5 months of age, she sustained the first of a long series of recognized pathologic fractures, this one involving the right femur. The fracture was treated by the application of a plaster cast, and union of the fragments took place inside of six weeks. Within the next twelve months two more fractures occurred after relatively slight trauma, one of the right tibia and the other of the right femur. Closed reduction was employed successfully each time. By the time the girl was 4 years old the lower extremities had become seriously deformed; although she was able to walk unaided, her gait was clumsy and waddling. A second osteotomy was contemplated, but because of the apparently progressive nature of the predisposition to fracture, further investigation seemed warranted before surgical intervention was undertaken. At the suggestion of physicians at the New York Orthopaedic Hospital, the patient was taken to the Neurological Institute of New York, where studies during a period of two weeks led to the tentative opinion that the child had a neoplasm of the adrenal glands.

For two months after discharge the patient was treated in the department of endocrinology of the Vanderbilt Clinic. At the end of this time she broke her right femur, and she was brought by the parents to the Babies Hospital on April 29, 1931. She was then 4 years and 7 months of age.

Physical Examination.—The patient weighed 22 Kg. (48 pounds) and was well nourished but not obese; her height was 112 cm. (45 inches). She was mentally alert and easily approachable, responding eagerly to social contacts. Sexual maturity appeared to be complete. The breasts were fully developed; the nipples were well differentiated and surrounded by large, deeply pigmented

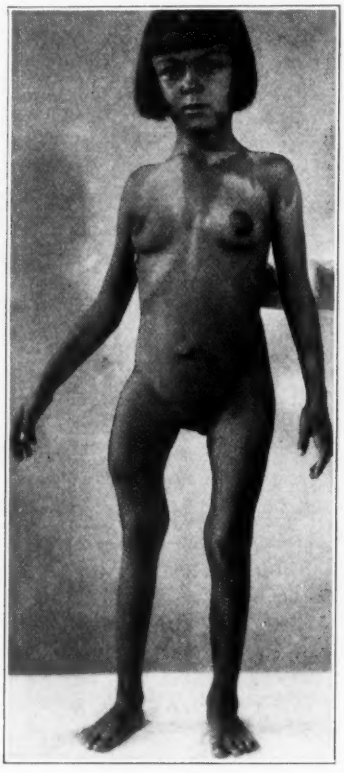

Fig. 1.—The patient in October 1931 (chronological age, 5 years and 1 month). The visible features of precocious sexual development are well marked. The complexion is swarthy. Brown pigmentation is distributed in a maplike manner over the upper portion of the left side of the thorax and the neck and is also evident in the pudendal region. The right arm and leg are deformed. Although the legs are rather hairy, true hypertrichosis is absent.

areolas. A sparse growth of coarse black hair was present about the genitals and in the axillae. The structures of the pudendal region exhibited advanced development. The uterus was easily felt; the cervix was about 1 cm. long, and the body was 5 cm. long. Each ovary was determined by palpation to be about 2 cm. in diameter; the left was slightly larger than the right.

The complexion was swarthy. The skin was of delicate texture and felt warm and moist. Scattered diffusely over the surface of the body were irregularly outlined patches of coffee-colored pigment. The texture of these patches was identical with that of the rest of the integument; they were not raised above the surface of the skin, and they did not exhibit increased vascularity. Anteriorly and posteriorly the pigment was more profuse on the left side than on the right (figs. 1 and 2).

The skeleton was deformed. The head appeared larger than normal, and the left maxillary region was more prominent than the right. The right femur was

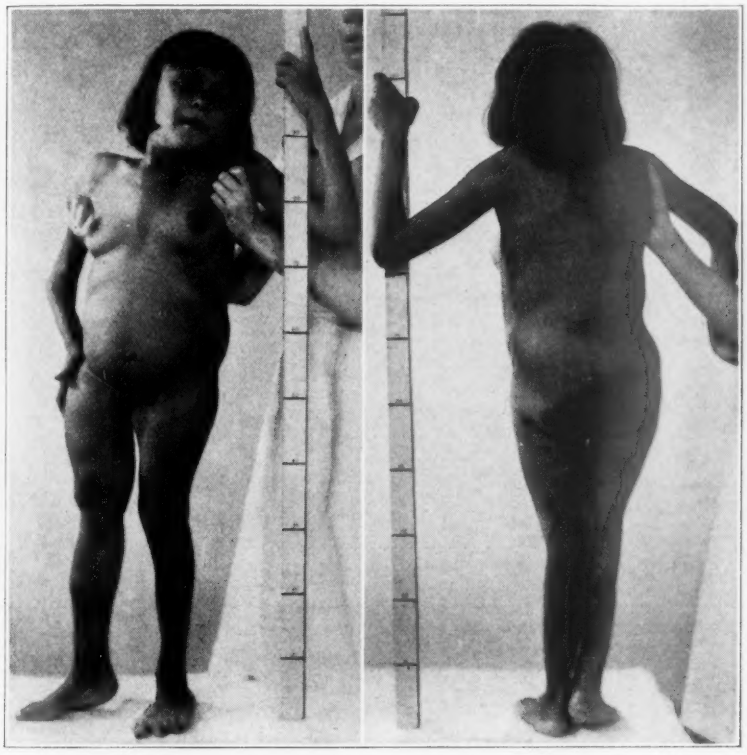

Fig. 2.—The patient in November 1935 (chronological age, 9 years and 2 months). The skeletal deformities have resulted in increasing physical incapacity. The secondary sex characters and the pigmentary disturbances have not changed. The pigment is distributed fairly symmetrically over the posterior aspect of the trunk, but the left leg exhibits more pigmentation than the right.

curved laterally, and the right leg was shorter than the left. The right forearm was angulated at the juncture between the proximal and the distal half. The sites of previous operations were indicated by the presence of surgical scars and roughening of the bone along the anterior aspects of both tibias. The hands were of normal appearance and presented no features suggestive of acromegaly.

The hair of the head was jet black, copious and silky. Although the arms and legs showed a moderate amount of soft hair, hypertrichosis of the face and

the extremities was absent. The superficial veins of the scalp were prominent. The sight and the hearing were intact, and the optic fundi presented no abnormalities. The dentition had been greatly accelerated. Most of the teeth belonged to the permanent denture; they were irregularly arranged and extremely carious. A soft systolic murmur, heard over the entire precordium, was loudest when the patient was in the recumbent posture. Otherwise the heart and the lungs were normal. The systolic blood pressure was 110 mm. of mercury and the diastolic pressure was 60 mm. The pulse was rapid (120 beats per minute) and bounding. The edge of the liver was felt just below the costal margin; the organ was firm and smooth. The spleen extended 2 cm. below the costal margin and also was firm. Both kidneys were palpable but seemed neither enlarged nor displaced downward. The thyroid gland was not felt. Although an equivocal cracked pot sound was elicited over the calvarium, other signs of increased intracranial pressure were

TABLE 1.—*Results of Chemical Examination of the Blood When the Patient Was 4 Years and 8 Months of Age*

	5/5/31	5/15/31
Whole blood, Mg.*		
Nonprotein nitrogen	33.4	30.0
Creatinine	1.4	1.4
Chlorides (as sodium chloride)	490.0	520.0
Sugar (while fasting)	111.0	123.0
Cholesterol	133.0	132.0
Serum, Mg.*		
Calcium	10.4	10.4
Phosphorus	4.5	3.8
Bilirubin	0.45	
van den Bergh reaction	Indirect	
Plasma, Gm.*		
Albumin	3.81	4.32
Globulin	2.48	2.52
Fibrinogen	0.51	0.51
Carbon dioxide-combining power, volumes per cent	43.2	39.8

* Per hundred cubic centimeters.

absent. Examination of the central and the peripheral portion of the nervous system revealed no noteworthy abnormalities.

Laboratory Examination.—The concentration of hemoglobin was 14.8 Gm. per hundred cubic centimeters (Sahli); the erythrocytes numbered 5,020,000. The leukocyte count was 11,000 per cubic millimeter; 68 per cent of the cells were polymorphonuclear and 32 per cent lymphocytic. Examination of the urine yielded negative findings. Ketone bodies were not detected. The results of chemical examination of the blood are shown in table 1.

A dextrose tolerance test, in which 39 Gm. of dextrose (1.77 Gm. per kilogram of body weight) was administered by mouth, gave the following results:

Reducing Substance Present in the Whole Blood, Milligrams per Hundred Cubic Centimeters

After fasting	123
One hour after administration of dextrose	141
Two hours after administration of dextrose	126

The urine which was collected during the first hour contained 0.08 Gm. of reducing substance per hundred cubic centimeters and that collected during the second hour 0.14 Gm. The Mantoux tuberculin test was negative when 0.1 mg. of old tuberculin prepared by the New York city health department was used. The Kahn test of the serum, for syphilis, was also negative. The basal metabolic rate was found to be 34 per cent above the normal as given in the standards of Talbot, Wilson and Worcester.[1] These norms are based on weight alone; they were chosen, rather than standards which take account of surface area or sitting height, because of the severe deformity of the child's skeleton.

Roentgen Examination.—The description which follows refers to the examination made in May 1931, when the child was 4 years and 8 months of age. Films were selected for reproduction which showed the pathologic findings most clearly, without regard to the time when they were obtained.

In the skull (fig. 3) the normal density of the calvarium was irregularly diminished, in a manner which produced a mottled, moth-eaten appearance; in

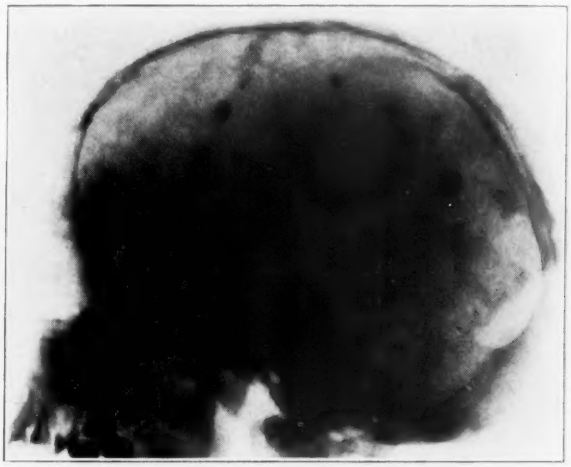

Fig. 3.—The skull in October 1935 (chronological age, 9 years; skeletal age, from 18 to 22 years). The density of the calvarium is irregularly diminished, and the finer markings are difficult to distinguish. The base of the skull is sclerotic, and the apparent volume of the sella turcica is decreased.

this region the finer markings were either poorly defined or invisible. The base of the skull appeared sclerotic, and the apparent volume of the sella turcica was diminished.

Cystlike diminution of density was the dominant lesion in the right forearm (fig. 4). In some places the individual shadows of negative density were regular in outline, clearly defined and sharply demarcated one from another; in other places the margins were irregular, difficult to distinguish and frequently merged with the boundaries of other cystlike areas. In several places the surface of the bone overlying these areas exhibited fusiform expansion; at numerous points

1. Talbot, F. B.; Wilson, E. B., and Worcester, J.: Standards of Basal Metabolism of Girls (New Data) and Their Use in Clinical Practice, J. Pediat. 7:655 (Nov.) 1935.

the cortex appeared to be ill defined or absent. The bones of the carpus (fig. 5) and the phalanges of the hand were similarly affected: The phalanges had lost their curving contour and were thick and rectangular; their density was diffusely increased, although they contained many cystlike shadows of negative density. The right humerus appeared somewhat osteosclerotic, particularly in its proximal portion (fig. 4), where the increase in density approached that observed in cases of Albers-Schönberg's disease. The contour of the bone was slightly altered,

Fig. 4.—The right arm in May 1932 (chronological age, 5 years and 9 months; skeletal age, from 12 to 14 years). The forearm is diffusely osteoporotic and shows multiple cystlike shadows, interruption of the continuity of the cortex and expansion of the medullary canal. The radius and the ulna are bowed. The proximal portion of the humerus is sclerotic.

and cystlike shadows were not present. The left arm (fig. 6) appeared relatively normal in contrast with the right; however, the left carpus and hand were indistinguishable from the right.

The appearance of the right femur (fig. 7) was bizarre: Neither the contour nor the structure of this member bore the slightest resemblance to that of normal bone. Although the head of the femur was recognizable as such, the

remainder of the bone was shortened, expanded and distorted to an extraordinary degree. The normal pattern of the finer markings of the bone was replaced by an indescribable confusion of shadows of greater and lesser density, which resulted in an appearance best described by likening it to a column of slowly ascending smoke. The right tibia and fibula (fig. 8) were similarly, although not so severely, affected. The feet bore a close resemblance to the hands.

Of all the bones of the skeleton, the clavicles alone appeared to be intact. Lesions were present in the ribs, particularly those of the left half of the thorax, and in the scapulae. In the spine the changes were principally of a sclerosing nature, although many cysts were present.

Comparison of the right and the left half of the skeleton demonstrated that the lesion, while not strictly unilateral, was strikingly asymmetrical. This fea-

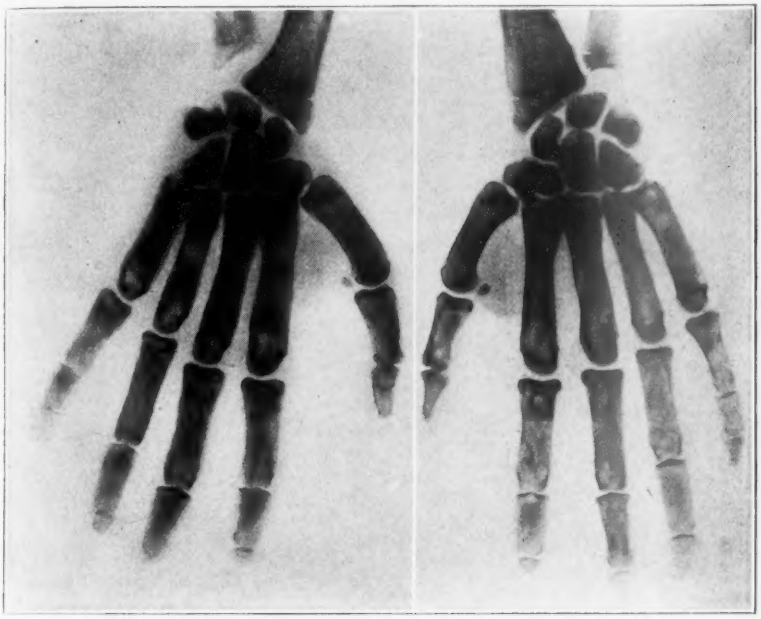

Fig. 5.—The right and the left hand in October 1935 (chronological age, 9 years and 1 month; skeletal age, from 18 to 20 years). The lesion is almost symmetrical. It consists of both increase and decrease of density, alteration of the shape of the bones and annular cystlike shadows. Accelerated maturity of the skeleton is obvious.

ture was illustrated in the pelvis (fig. 9): The right innominate bone appeared gnarled and fragile; the left ilium and ischium and the left half of the pubis were relatively normal.

With few exceptions, the zones of preliminary calcification were intact; however, this was not true in the right femur, where the site of the distal epiphysis was indistinguishable from the remainder of the bone.

The right femur, the right tibia and both fibulas exhibited scars and angulation indicative of previous fracture.

A comprehensive description of the state of the centers of ossification is unnecessary. The following features are mentioned as an index of the degree of skeletal maturity: Eight bones were visible in each carpus and seven in each tarsus; the individual bones exhibited a high degree of penetration into the primitive cartilage. A sesamoid bone was present at the distal end of the metacarpal bone of the left thumb. The styloid process of the ulna exhibited clear-

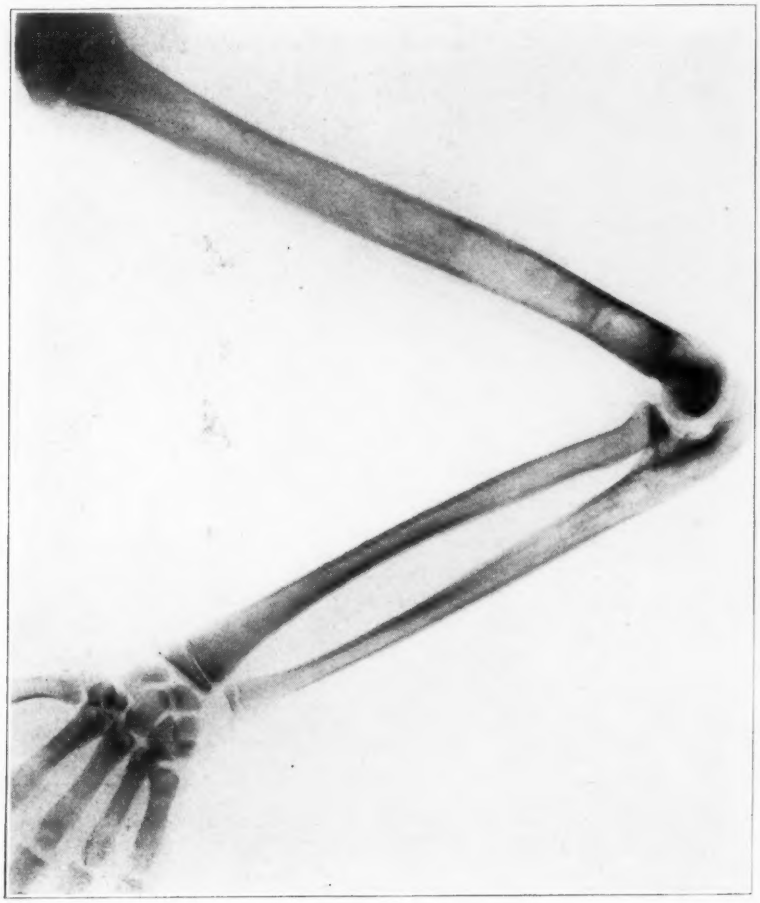

Fig. 6.—The left arm in May 1932 (chronological age, 5 years and 7 months). By comparison with the right arm (fig. 4), the left appears relatively normal.

cut differentiation. Many of the epiphyses had commenced to fuse with their corresponding shafts. Roentgenograms of the jaws revealed accelerated calcification and eruption of the permanent teeth; the second molars came through at the age of 6 years, and the third molars, between the ages of 8 and 9 years.

The lungs appeared normal. The shadow of the heart was slightly enlarged to the left.

Summary and Interpretation: The roentgen findings were those of a generalized systemic disease of the skeleton. Cystlike rarefaction of the bone consti-

tuted the most conspicuous abnormality. Associated with this were varying degrees of irregularly distributed osteoporosis and osteosclerosis, numerous deformities of the outline and the architecture of individual bones, evidence of previous fracture, precocious development of numerous centers of ossification and accelerated calcification and eruption of the teeth. Although no member of the skeleton was entirely spared, the lesion was decidedly asymmetrical, being

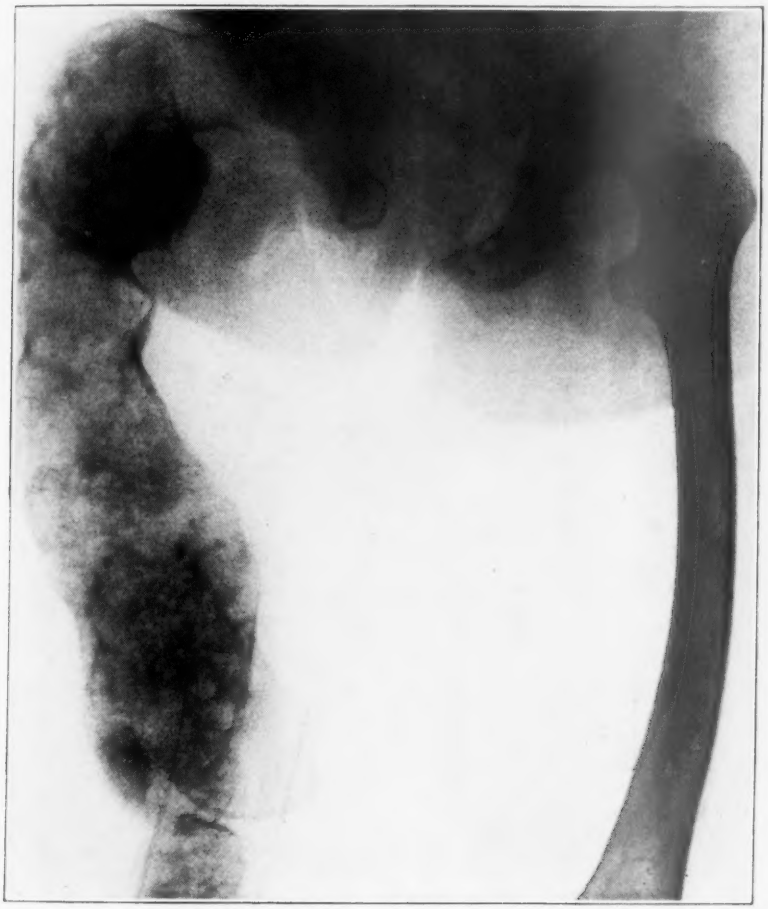

Fig. 7.—The roentgen appearance of the bones of the thighs in October 1935 (chronological age, 9 years and 1 month). The right femur can scarcely be recognized as a bone; the left appears relatively intact.

more extensive and more severe on the right than on the left. A descriptive diagnosis of osteodystrophia fibrosa, possibly of the von Recklinghausen variety, was submitted; stress was placed on the resemblance of the changes in the skull to those seen in Paget's disease. On the basis of the state of development of the skeleton, the child's age was estimated to be between 10 and 12 years. As previously mentioned, her chronological age was about 5 years.

Course in the Hospital.—After two months of immobilization the right leg had united firmly and the child was able to bear weight on it. Considerable angulation had taken place between the proximal and the distal fragment; this made walking more clumsy and difficult than before. During the two months which she spent in the hospital, the patient exhibited moderate emotional instabil-

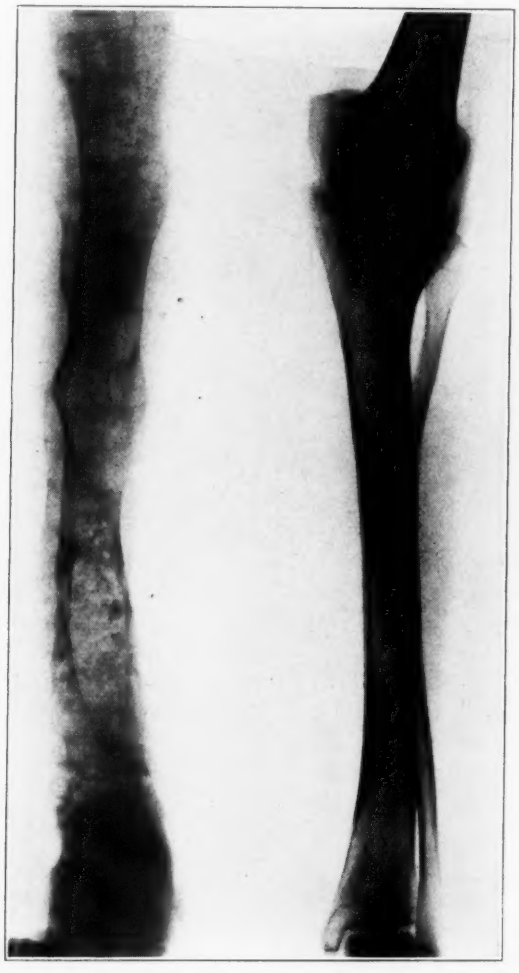

Fig. 8.—The legs in October 1935 (chronological age, 9 years and 1 month). Although lesions are present in both tibias, they are much more severe on the right. The curvature of the left fibula is due to previous fractures, and the irregularity of the outline of the right tibia, in part at least, to the same cause.

ity, a tendency to diaphoresis and slight tachycardia. These phenomena were not commented on especially at the time, although they are of importance in the light of later developments.

Subsequent Clinical Course (From the Fifth to the Tenth Year of Age).—During the five years which has elapsed since the patient first came to our attention, she has been admitted to the Babies Hospital seven times, because of recurrent pathologic fracture, for diagnostic investigations and, finally, for mastoidectomy.

Her clinical course (fig. 10) has been characterized by progressive deterioration of the skeleton and by the emergence and intensification of signs of hyperthyroidism. During the period under discussion she has sustained nineteen recognized fractures and probably many more which have escaped detection. The majority of these fractures have affected the right half of the skeleton. Operative treatment has never been required; without exception the bones have united within from four to six weeks with the aid of immobilization. The deformity of stature

Fig. 9.—The pelvis in October 1931 (chronological age, 5 years and one month). The lesion is asymmetrically distributed in the two halves of the pelvis.

which has resulted from the long succession of fractures has been exaggerated by progressive collapse of several of the spinal vertebrae. Despite the trial of a series of supporting devices, the child is unable to get about by herself and spends most of her time in bed.

Roentgenographic examination in October 1935, at the age of 9 years and 1 month, revealed unremittent progression of the lesions which were observed in 1931. The cystlike disturbances in the right ulna (fig. 11) had produced expansion of the distal end of the bone. The sclerosing nature of the lesion in the region of the right elbow was more prominent. The left arm, which had previously appeared relatively normal (fig. 6), now exhibited evidence of extensive involvement (fig. 12). The right femur had undergone further deformity. Collapse of several spinal vertebrae had occurred (fig. 13). Even the clavicles exhibited

rarefying alterations. The left femur, alone, presented an approximately normal appearance. Many of the epiphyses had become fused with the shafts. The third molars had erupted. The degree of maturity of the skeleton was equal to that of a girl between 18 and 22 years of age.

As previously intimated, manifestations of latent hyperthyroidism were present during the fourth year of life. By the fifth year the thyroid gland had become easily palpable; nervousness and sweating were more evident; the systolic blood pressure had increased to 150 mm. of mercury, while the diastolic pressure had remained in the neighborhood of from 50 to 60 mm.; moderate tachycardia persisted, and the basal metabolic rate had risen to 44 per cent above normal. At this time Dr. Emil Goetsch, who saw the patient in consultation, detected a small nodule in the region of the left inferior pole of the thyroid gland. This was later found by histologic examination to be composed of adenomatous thyroid tissue. By the time the patient was 9 years old, hyperthyroidism was obvious. Although the child exhibited no exophthalmos, marked tremor of the hands was

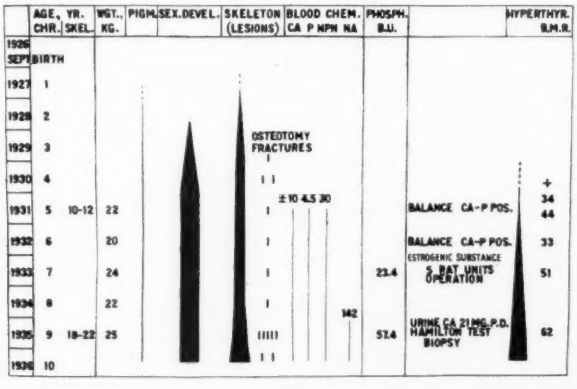

Fig. 10.—Chart showing the child's course during the first nine years of life. The passage of time is represented from above downward and the individual clinical items from left to right. The increasing width of the black columns indicates progression of the phenomenon to which they refer; the unchanging width of the lines representing pigmentation (*Pigm.*) and the results of chemical examination of the blood indicate that we are aware of no quantitative variation in these features. The dotted lines at the top of three of the columns denote that our information covering these periods is incomplete. *Chr.* indicates chronological, and *Skel.*, skeletal, both referring to the age in years. The weight is given in kilograms. Calcium and phosphorus are reported in milligrams per hundred cubic centimeters of serum; sodium in milliequivalents per liter of serum, and nonprotein nitrogen in milligrams per hundred cubic centimeters of whole blood. *Phosph.* indicates serum phosphatase activity; *B. U.*, Bodansky units; *Hyperthyr.*, hyperthyroidism, and *B. M. R.*, basal metabolic rate. Each vertical bar under *Fractures* represents a separate fracture.

present and the bed clothing was frequently drenched by perspiration; the thyroid gland had become somewhat enlarged and was firm and nodular; a thrill and bruit could be appreciated over the left side of the thyroid isthmus, and the basal

metabolic rate had reached 65 per cent above the normal according to the Talbot-Wilson standards. The pulse was full and bounding and the respirations rapid and shallow (table 2). The vital capacity was diminished.

During these five years the visible sex characters and the pigmentation of the skin remained unaltered. The patient continued to menstruate with increasing regularity. Periods occurred from six to eight times a year, being separated by

Fig. 11.—The right arm in October 1935 (chronological age, 9 years and 1 month; skeletal age, from 18 to 22 years). Further expansion has taken place in the distal end of the ulna during the three and one-half years which have elapsed between the taking of this film and the taking of that reproduced in figure 4.

intervals of from six to eight weeks, and lasted from three to five days. The loss of blood was usually moderate, although on two occasions severe metrorrhagia occurred. The child never complained of menstrual pain. We have no information concerning the presence or absence of sexual desire.

The child was 9 years and 8 months old when she was examined in May 1936. She weighed 25 Kg. (55 pounds) and was 116 cm. (46.4 inches) in height. She was well nourished but deformed. The head still appeared rather large, and the left side of the face was more prominent than the right. The superficial veins of the forehead remained dilated. The fine texture of the hair was unchanged. The eyes were slightly prominent and showed slight lid lag; the optic media and the fundi were normal. Dental caries had become more severe. The thyroid

Fig. 12.—The left arm in October 1935 (chronological age, 9 years and 1 month). The progressive nature of the disease is illustrated by the presence of large areas of negative density in the distal two thirds of the left humerus. Although these were discernible in previous examinations (fig. 6), they were relatively inconspicuous in the long bones of the left upper extremity.

gland was enlarged, firm and nodular; a thrill and an accompanying bruit were present over the entire gland. The heart, although only slightly enlarged, was overactive; the rate was 120 beats per minute. A systolic murmur was heard just inside the point of maximal impulse. The radial pulses were full and bound-

ing. The systolic blood pressure was 125 mm. of mercury in the right arm and the diastolic pressure 70 mm.; in the left arm the systolic pressure was 120 mm. and the diastolic pressure 60 mm. Both levels were somewhat higher in the legs. The liver extended 2 cm. below the ribs but was of normal consistency. The spleen was felt about 3 cm. below the costal margin and was firmer than normal. The lower pole of the left kidney was palpated at the end of deep inspiration. Neither the right kidney nor the bladder were felt. The function of the cranial nerves was intact. The deep and the superficial reflexes were normal in all four

Fig. 13.—The lumbar portion of the spine in October 1935 (chronological age, 9 years and 1 month). Several of the vertebral bodies have collapsed. The laminae and the spinous processes are extremely osteoporotic.

extremities. No loss of sensation could be demonstrated over the surface of the body or in the arms or legs. The rectal and the vesical sphincter functioned normally.

Special examination of the eyes revealed a visual acuity of 20/20 in the right eye and 20/30 in the left eye. It was not possible to plot the visual fields accurately, but the roughly drawn outlines seemed normal. The blindspots were normal in position and shape.

Audiometric examination demonstrated equal loss of hearing in both ears; this varied from 40 per cent for frequencies of 64 vibrations per second to 10

per cent for frequencies of 8,192 vibrations per second. This response was interpreted to indicate a mild, bilateral conduction deafness, probably in the middle ear.

The consulting gynecologist found the uterus to be approximately 5 cm. long. Each of the ovaries was about 1 cm. in diameter. The right ovary remained slightly larger than the left. The fallopian tubes could not be felt.

The electrocardiographic record was normal.

The child's scores on the Stanford-Binet test, the Terman test and the Goodenough drawing test were virtually equal and indicated a mental age of 7 years and 5 months; the ratio between her mental age and her chronological age (9 years and 2 months) was 0.82. It will be recalled that at the age of 4 years and 6 months she had an intelligence quotient of 1.13. Her score in the Terman test at that time indicated a mental age of 5 years.

TABLE 2.—*Observations on the Rate of the Pulse and the Respiration During Periods Spent in the Hospital* *

Date	Age Yr.	Age Mo.	Number of Observations	Mean	Standard Deviation	Coefficient of Variability
4/29/31	4	7	Pulse 164	107.6	±15.4	14.3
6/29/31			Respiration 163	23.9	± 3.4	14.4
10/ 7/31	5		Pulse 77	111.1	±11.5	10.3
11/14/31			Respiration 77	26.7	± 3.6	13.4
3/14/32	5	6	Pulse 128	113.6	± 8.8	7.6
5/19/32			Respiration 126	25.0	± 4.0	16.0
6/ 7/33	6	9	Pulse 127	110.3	±12.0	10.9
7/31/33			Respiration 141	24.8	± 4.4	17.7
10/26/35	9	1	Pulse 137	108.5	±12.4	10.5
12/19/35			Respiration 129	24.7	± 4.3	17.2
12/ 5/36 †	10	3	Pulse 48	137.3	±11.9	8.6
12/23/36			Respiration 48	36.5	± 7.1	19.5

* Evidence of acute infection was not apparent at the time of these observations.
† Chronic mastoiditis; before operation

Additional Diagnostic Investigations.—Numerous hematologic examinations have yielded consistently normal results (table 3). The urine has been examined repeatedly by routine methods. The twenty-four hour volume has averaged about 800 cc. and has never exceeded 1,200 cc. The specific gravity has tended to be high, ranging between 1.020 and 1.030. A faint trace of albumin has been discovered frequently. A reducing substance of an unidentified nature has been found from time to time; we have assumed that this substance was dextrose. Its concentration has generally been reported as a trace, but on a few occasions it has been as high as ++++. The formed elements of the urine have never been abnormal in type or amount. Six examinations for Bence-Jones' protein have yielded negative results. Ketone bodies have been present only during acute illness.

An intravenous urogram (with diodrast) in November 1935, when the child was 9 years and 2 months old, failed to reveal abnormalities in the form of the renal pelves or in the shape or the position of the kidneys. The dye appeared in lesser concentration on the left side than on the right; this inequality suggested impairment of the excretory function of the left kidney. No evidence has been obtained to confirm this interpretation, and the fortuitous inconsistencies of intravenous pyelography must be kept in mind.

The blood has been examined chemically on numerous occasions (table 4). With few exceptions, which will be touched on later, the examinations have yielded consistently normal results.

Balance studies of the metabolism of calcium and phosphorus were made twice. The first was carried out when the child was 5 years old.

TABLE 3.—*Data from Representative Hematologic Examinations When the Patient Was Between 4 Years and 7 Months and 9 Years and 7 Months Old*

Date	Age Yr.	Age Mo.	Hemoglobin, Percentage (Sahli) *	Red Blood Cells	White Blood Cells	Polymorphonuclears, Percentage	Lymphocytes, Percentage	Monocytes, Percentage	Eosinophils, Percentage
April 1931	4	7	87	5,020,000	11,000	68	32	..	..
October 1931	5	1	80	4,040,000	8,850	50	48	1	..
April 1932	5	7	82	4,472,000	7,300	53	42	1	1
June 1933 †	6	9	90	4,464,000	8,500	62	32	1	3
October 1935	9	1	84	4,648,000	7,700	59	34	1	5
April 1936 ‡	9	7	96	4,600,000	10,000	76	15	3	4

* 100 per cent = 17 Gm. per hundred cubic centimeters.
† Bleeding time, 1½ minutes.
‡ Otitis media.

TABLE 4.—*Results of Chemical Examination of the Blood When the Patient Was Between 5 and 10 Years Old (See Also Tables 1 and 6)*

			Whole Blood, Mg. per 100 Cc.		Serum								Plasma Gm. per 100 Cc.		
					Mg. per 100 Cc.										
Date	Age Yr.	Age Mo.	Nonprotein Nitrogen	Sugar	Calcium	Phosphorus	Chloride	Cholesterol	Sodium	Total Fixed Base, Milliequivalents per Liter	Phosphatase, Bodansky Units per 100 Cc.	Carbon Dioxide-Combining Power, Volumes per cent	Albumin	Globulin	Fibrinogen
8/20/31	4	11	....	...	9.8	...	...	...	...	...	....	....	...	...	...
10/26/31	5	1	32.6	...	10.6	3.2	...	...	...	...	....	....	4.1	1.8	0.5
11/ 9/31	5	2	47.7	...	10.8	3.3	...	...	...	...	....	....	3.7	2.1	0.3
3/23/32	5	6	30.1	96	10.6	3.7	...	...	...	...	....	37.4	4.2	1.2	0.3
4/14/32	5	6	29.8	107	10.4	3.6	...	...	...	...	....	35.6	4.4	1.7	0.4
4/23/32	5	7	31.7	83	9.4	3.1	...	...	...	...	....	32.0	...	...	...
7/10/33	6	10	34.9	...	9.3	3.0	...	...	137	...	23.4	....	...	...	...
4/24/35	8	8	30.2	...	9.6	3.2	...	...	141	150	....	43.2	...	...	...
10/31/35	9	1	34.6	81	9.6	3.1	623	145	...	...	57.4	....	3.3	2.0	...
4/10/36	9	8	....	...	8.6	3.3	...	...	134	146	....	....	..	....	...
12/ 9/36	10	3	28.1	116	8.9	2.3	552	143	...	...	58.0	51.6	3.9	1.9	0.4

Technic of the Balance Studies: The patient remained in bed. She received a diet of meat, vegetables, fruit, cereal, bread, butter and dried skimmed milk (Dryco). A twenty-four hour portion of the diet was estimated to contain 147 Gm. of carbohydrate, 71 Gm. of protein (3.5 Gm. per kilogram of body weight) and 58 Gm. of fat; it yielded 1,394 calories (68 calories per kilogram of body weight), of which 42 per cent was supplied by carbohydrate, 20 per cent by protein and 38 per cent by fat. Chemical analyses of suitably prepared

aliquot samples of the diet on three separate occasions showed the average twenty-four hour intake of calcium to be 0.591 Gm. and that of phosphorus to be 0.992 Gm. The ratio of calcium to phosphorus in the diet was 0.59. On the basis of these analyses, it was computed that the patient ingested 0.029 Gm. of calcium and 0.050 Gm. of phosphorus per kilogram of body weight daily. The potential acid of the diet was estimated from Sherman's figures [2] to be 38 cc. of tenth-normal solution and the base to be 31 cc. of tenth-normal solution. Distilled water was used in cooking the food, and the patient was allowed up to 700 cc. of distilled water a day in addition to that used in preparing the food. The usual precautions were taken to ensure accuracy in weighing the food, and an approximation of quantitative chemical technic was used in collecting excreta. Fortunately, the child ate all that was offered. She vomited only once; the loss of calcium and phosphorus which occurred in this manner was determined by estimation and not by analysis. The measured diet was served for two weeks before the collection of urine and feces was begun. The individual metabolism periods were marked by the oral administration of powdered carmine.

The calcium content was determined by the titrimetric procedure of Fiske and Logan [3] and the phosphorus content by the colorimetric method of Fiske and Subbarow.[4] The urine was preserved with toluene. For urinary calcium, aliquots of 10 cc. were employed; these were ashed by heating with concentrated sulfuric and nitric acids. The urinary phosphorus content was determined directly in samples of 1 or 2 cc., which were not ashed. The stools were dried at 100 C. and then ground to a fine powder. Portions of stool dried at 95 C., which weighed 0.5 Gm., were ashed by heating with concentrated sulfuric and nitric acids and were then diluted to 50 cc. For calcium, aliquots of 10 cc. were taken; for phosphorus, the portions were of 1 or 2 cc. The food was prepared for analysis by destroying the organic matter with concentrated sulfuric and nitric acids. All determinations were done in duplicate and many in triplicate; values were accepted only when the results of duplicate analyses agreed within 2 per cent.

An abstract of the chemical data appears in table 5, and the data are shown graphically in figure 14.

The study was divided into eight consecutive periods, which lasted from three to six days each. During the first five periods, that is, during the first twenty days of the experiment, the balance of both calcium and phosphorus was positive. The patient retained an average of 0.0087 Gm. of calcium and 0.0065 Gm. of phosphorus per kilogram of body weight daily. The ratio between retained calcium and retained phosphorus was 1.34. Of the calcium which was excreted, 94.6 per cent appeared in the stools and 5.4 per cent in the urine. Of the phosphorus which was excreted, 50.2 per cent appeared in the stools and 49.8 per cent in the urine. During this period the child menstruated for one week and had mild diarrhea for five days. Neither of these occurrences appeared to influence the excretion of calcium or of phosphorus. Toward the end of the

2. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 3, New York, The Macmillan Company, 1927, appendix B, table II.

3. Fiske, C. H., and Logan, M. A.: The Determination of Calcium by Alkalimetric Titration: II. The Precipitation of Calcium in the Presence of Magnesium, Phosphate, and Sulfate, with Applications to the Analysis of Urine, J. Biol. Chem. **93**:211, 1931.

4. Fiske, C. H., and Subbarow, Y.: The Colorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375, 1925.

period the calcium content of the serum was found to be 10.6 mg. per hundred cubic centimeters and the inorganic phosphorus content 3.2 mg.

On the twenty-first day of the experiment and for four days thereafter the child was given subcutaneously 200 U. S. P. units daily of parathyroid extract,[5] which was equivalent to 10 units per kilogram of body weight daily. A total

TABLE 5.—*Metabolic Study of a Calcium and Phosphorus Balance (Child's Age, 5 Years)*

Daily Intake of Calcium and Phosphorus

	Calcium, Gm.	Phosphorus, Gm.
Milk	0.448	0.381
Other food	0.143	0.612
Total	0.591	0.993
Gm./Kg.	0.030	0.050

Ratio, calcium to phosphorus in diet: 0.60

Periods I to V inclusive (Oct. 12 to Nov. 1, 1931, inclusive: 20 days); average weight, 20,000 Gm.; no medication (fig. 14)

	Calcium		Mode of Excretion,	Phosphorus		Mode of Excretion,
Output	Per Period	Per Day	Percentage	Per Period	Per Day	Percentage
Urine	0.451	0.023	5.4	8.584	0.429	49.8
Stool	7.887	0.394	94.6	8.668	0.434	50.2
Total	8.338	0.417	100	17.252	0.863	100
Intake	11.824	0.591		19.850	0.993	
Balance	3.486+	0.174+		2.598+	0.130+	
Retention						
Mg. per Kg.	0.174	0.0087		0.130	0.0065	
Percentage of intake retained	29			13		

Ratio of calcium retained to phosphorus retained: 1.34

Periods VI and VII, disregarding the last 2 days of period VII, on which the balance again was positive (Nov. 2 to Nov. 10, inclusive: 8 days); parathyroid extract administered (table 6 and fig. 14)

	Calcium		Mode of Excretion,	Phosphorus		Mode of Excretion,
Output	Per Period	Per Day	Percentage	Per Period	Per Day	Percentage
Urine	1.324	0.166	25	4.308	0.538	54
Stool	4.063	0.508	75	3.743	0.467	46
Total	5.387	0.674	100	8.051	1.005	100
Intake	4.353	0.548		7.446	0.931	
Balance	1.034—	0.126—		0.605—	0.074—	
Loss						
Mg. per Kg.	0.052	0.006		0.030	0.0037	
Percentage of intake excreted	122			108		

Ratio of calcium excreted to phosphorus excreted ("depletion ratio"): 2.05

of 1,000 U. S. P. units was given within five days. The balance of both calcium and phosphorus became negative within three days after the first injection, and the maximal effect was observed on the fifth and sixth days, that is, twenty-four hours after the injections were discontinued. The balance did not become positive

5. The substance given was Parathyroid Extract-Lilly, then known as Parathormone-Lilly; it was measured in Collip's units, of which 40 are equal to 200 U. S. P. units.

until more than a week after the last injection. During the eight days from the first administration of the extract to the last day on which the balance was negative, the patient excreted 1.034 Gm. of calcium and 0.504 Gm. of phosphorus more than she ingested. The quotient of these two amounts, which may be termed the "depletion ratio," is 2.05. This is a close approximation of the ratio which exists between calcium and phosphorus in normal bone,[6] namely 2 to 2.26. During the eight day period 25 per cent of the excreted calcium was found in the urine and 75 per cent in the stools. Of the phosphorus which left the body, 54 per cent was recovered from the urine and 46 per cent from the stools.

During the five days on which parathyroid extract was given the serum calcium content rose markedly and the concentration of serum inorganic phos-

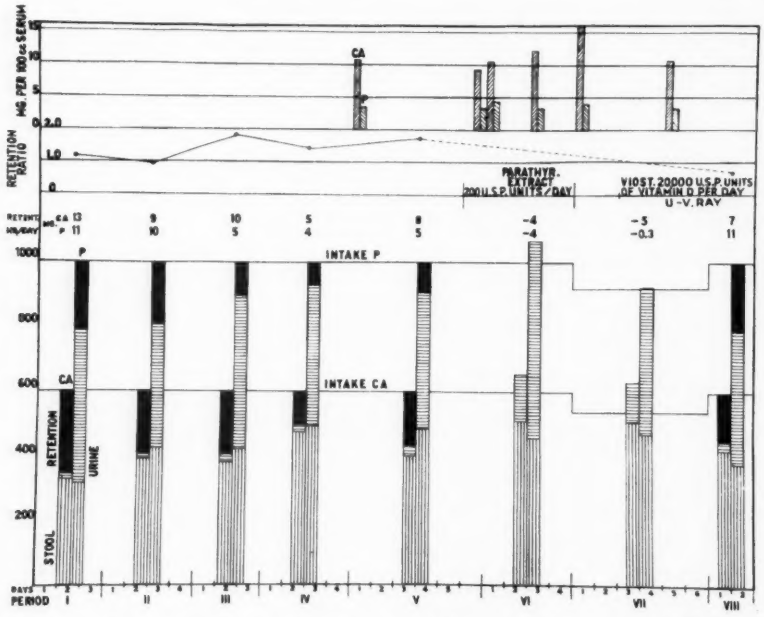

Fig. 14.—Chart showing the results of a balance study of the metabolism of calcium and phosphorus. The dotted line which passes through the periods when the balance was negative serves only to draw the eye to the small circle which represents the retention ratio during period VIII. *Viost.* indicates viosterol, and *U-V. Ray,* ultraviolet irradiation for approximately thirty minutes daily, front and back. The duration of the study was thirty-two days and the age of the patient 5 years.

phorus remained relatively unchanged (table 6). The administration of the extract was stopped because the child commenced to vomit.

During the last period (VIII) the balance of both calcium and phosphorus returned to positive. Although ultraviolet ray and viosterol (20,000 U. S. P.

6. Roseberry, H. H.; Hastings, A. B., and Morse, J. K.: X-Ray Analysis of Bone and Teeth, J. Biol. Chem. **90**:395, 1931. Bogert, L. J., and Hastings, A. B.: The Calcium Salts of Bone, ibid. **94**:473, 1931.

TABLE 6.—*The Behavior of the Serum Calcium and Serum Inorganic Phosphorus During a Period of Five Days, on Each of Which 200 U. S. P. Units of Parathyroid Extract Was Given*

Date, 1931	Parathyroid Extract, U. S. P. Units	Serum Calcium, Mg. per 100 Cc.	Serum Inorganic Phosphorus, Mg. per 100 Cc.
10/31		9.2	3.6
11/ 1	200	10.4	4.3
11/ 2	200	....	...
11/ 3	200	....	...
11/ 4	200	12.2	3.3
11/ 5	200	....	...
11/ 6		16.0	4.0
11/ 7		....	...
11/ 8		10.8	3.3
	Total.....1,000		

TABLE 7.—*Balance Study of Calcium and Phosphorus Metabolism (Child's Age, 5 Years and 6 Months; and Weight, 20 Kg.); Study II (March 24 to April 10, Inclusive, 1932: 17 Days)*

Diet: Bread, cereal, meat, vegetables, fruit, dried whole milk (Klim, 42 Gm. daily in 300 cc. of distilled water), distilled water up to 700 cc. daily in addition to that used in cooking, no added vitamin D

Daily Intake of Calcium and Phosphorus

	Calcium, Gm.	Phosphorus, Gm.
Milk	0.396	0.291
Other food	0.104	0.582
Total	0.500	0.873
Gm./Kg.	0.025	0.044

Ratio: Calcium to phosphorus in diet: 0.57

Period I (March 24 to March 29, inclusive: 6 days)

Output	Calcium		Mode of Excretion, Percentage	Phosphorus		Mode of Excretion, Percentage
	Per Period	Per Day		Per Period	Per Day	
Urine	0.112	0.019	4	2.653	0.442	33
Stool	2.410	0.401	96	1.287	0.215	67
Total	2.522	0.420	100	3.940	0.657	100
Intake	3.000	0.500		5.238	0.873	
Balance	0.478+	0.080+		1.298+	0.216+	
Retention Mg./Kg.	0.024	0.0040		0.065	0.0108	
Percentage of intake retained	16			25		

Ratio of calcium retained to phosphorus retained: 0.38

Period II (March 30 to April 10, inclusive: 11 days)

Output	Calcium		Mode of Excretion, Percentage	Phosphorus		Mode of Excretion, Percentage
	Per Period	Per Day		Per Period	Per Day	
Urine	0.247	0.022	5	4.339	0.394	50
Stool	4.803	0.437	95	4.300	0.391	50
Total	5.050	0.459	100	8.639	0.785	100
Intake	5.500	0.500		9.604	0.873	
Balance	0.450+	0.041+		0.965+	0.088+	
Retention Mg./Kg.	0.023	0.0021		0.048	0.0041	
Percentage of intake retained	8			10		

Ratio of calcium retained to phosphorus retained: 0.47

units of vitamin D per day) were administered during this period, the experiment was terminated before it became possible to evaluate the effect of these measures.

A second, shorter, study was carried out six months later, in March 1932, when the child was 5 years and 6 months of age. Dried whole milk (Klim) was used instead of dried skimmed milk. The excreta were analyzed for calcium by the gravimetric method of McCrudden.[7] Larger samples were used; otherwise the technic was the same as that of the previous experiment. The results, which appear in table 7, are similar to those obtained six months earlier.

In November 1935, when the child was 9 years and 2 months of age, serial determinations were made of the daily excretion of calcium in the urine by the gravimetric technic of Washburn and Shear.[8] During this study the child received the usual ward diet. This supplies an average of approximately 1.2 Gm. of calcium and 1.1 Gm. of phosphorus per day. The excretion of calcium in the urine under these circumstances is shown in table 8. The values obtained in this relatively crude experiment were similar to those yielded by the two balance studies.

The results of these studies are quantitatively similar to those obtained by Daniels and her associates with normal children.[9] During the period in which

TABLE 8.—*The Excretion of Calcium in the Urine on Six Successive Days While the Child Was on the Ward Diet and Receiving No Medication (Age, 9 Years and 2 Months); Approximate Daily Intake; Calcium 1.2 Gm. and Phosphorus 1.1 Gm.*

Date, 1935	Length of Period, Hours	Volume of Urine, Cc.	Total Calcium, Gm.	Concentration of Calcium, Mg. per 100 Cc. of Urine
11/15	12	148	0.0106	7.2
11/16	24	340	0.0167	4.9
11/17	24	248	0.0197	7.8
11/18	24	650	0.0236	3.6
11/19	24	815	0.0290	3.6
11/20	24	1,040	0.0179	1.7
			Mean 0.0213 (per 24 hours)	

the specimens of urine for the last-mentioned analyses were being collected, a series of titrations of the concentration of parathyroid hormone in the patient's whole blood was made according to the biologic technic described by Hamilton and Schwartz.[10] We experienced more difficulty with the method than the published statements of the authors[11] and those of Shelling and Remsen[12] had

7. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 2, p. 761.

8. Washburn, M. L., and Shear, M. J.: Composition of Bone: XIII. Direct Gravimetric Determination of Ca, Mg, and PO_4, J. Biol. Chem. **99**:21, 1932.

9. Daniels, A. L.; Hutton, M. K.; Knott, E.; Everson, G., and Wright, O.: Relation of Ingestion of Milk to Calcium Metabolism in Children, Am. J. Dis. Child. **47**:499 (March) 1934.

10. Hamilton, B., and Schwartz, C.: A Method for the Determination of Small Amounts of Parathyroid Hormone, J. Pharmacol. & Exper. Therap. **46**: 285, 1932.

11. Hamilton, B., and Schwartz, C.: Rickets and Hyperparathyroidism, Am. J. Dis. Child. **46**:775 (Oct.) 1933.

12. Shelling, D. H., and Remsen, D.: Renal Rickets: Report of a Case Showing Four Enlarged Parathyroids and Evidence of Parathyroid Hypersecretion, Bull. Johns Hopkins Hosp. **57**:158, 1935.

led us to anticipate. However, in two out of three tests (fig. 15), each made with 10 cc. of the patient's whole blood, the curve we obtained resembled that which Hamilton and Highman [13] described for normal adults. The third test was unsatisfactory for technical reasons.

Ethel Benedict Gutman determined the serum phosphatase activity by the Bodansky method [14] on three occasions. The values, which appear in figure 8 and table 4, are considerably in excess of the normal either for children (up to 12 or 15 units per hundred cubic centimeters) or for adults (up to 5 units per hundred cubic centimeters).

Two surgical efforts have been made to throw light on the diagnosis. The first of these was an exploration of the neck in search of a tumor of the parathyroid bodies; this was done when the child was about 7 years old. The posterior surface of the right lobe of the thyroid gland was examined carefully,

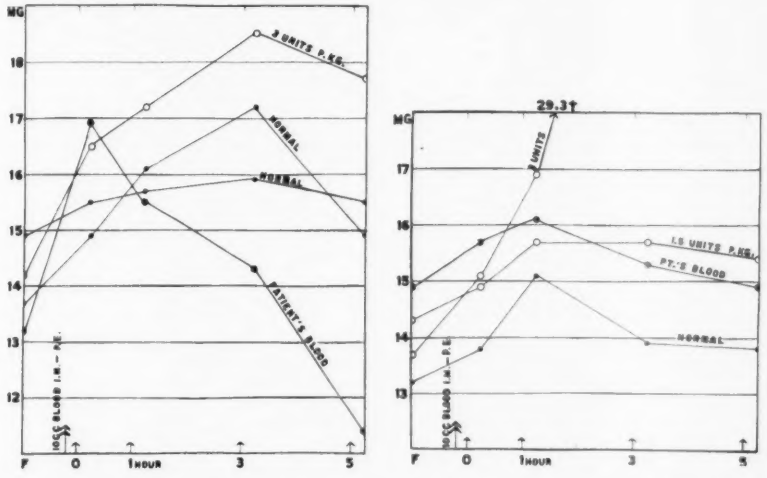

Fig. 15.—Chart showing the results of the Hamilton test (chronological age, 9 years and 2 months). The serum calcium content in milligrams per hundred cubic centimeters is represented on the ordinate and the time on the abscissa. The curves designated *Normal* were obtained by gavaging 2 kilogram rabbits with 0.276 Gm. of calcium chloride (0.1 Gm. of calcium) four times, the last three gavages being one, three and five hours, respectively, after the first gavage. Samples of blood were removed from the ear vein fifteen minutes after each gavage. The curves labeled *1.5 Units P. Kg.* (per kilogram of body weight) and *3 Units P. Kg.* show the results obtained when these amounts of parathyroid extract (U. S. P. units) were injected intramuscularly just before the first gavage. In the test 10 cc. of the patient's whole blood was substituted for the parathyroid extract. One rabbit died, presumably because calcium chloride was accidentally introduced into the lungs.

13. Hamilton, B., and Highman, W. J.: A Test for Abnormally Large Amounts of Parathyroid Hormone in the Blood, J. Clin. Investigation **15**:99 (Jan.) 1936.

14. Bodansky, A.: Phosphatase Studies: II. Determination of Serum Phosphatase; Factors Influencing the Accuracy of the Determination, J. Biol. Chem. **101**:93, 1933.

but no parathyroid tissue was recognized. However, on the posterior and lateral aspect of the lower pole of the left lobe of the thyroid gland a small nodule was encountered, which was firm, discrete and partially encapsulated. On the erroneous assumption that this was a hyperplastic parathyroid body, further search was abandoned; neither the isthmus of the thyroid nor the superior portion of the mediastinum was explored. The thyroid gland and the structures contiguous to it appeared normal. Histologic examination of the nodule revealed that the structure was not that of parathyroid tissue but was that of adenomatous hyperplasia of the thyroid cells.

In November 1935, when the child was 9 years and 2 months of age, two small fragments of bone were removed for histologic examination. The first was

Fig. 16.—Histologic features of a specimen of bone removed from the anterior aspect of the midportion of the right femur (fig. 7). Uncalcified cartilage is seen in the left upper corner of the photograph and calcified cartilage toward the center. On the left, just below the center, is a small spicule of well differentiated bone; on the right, just above the center, a curved spicule composed of calcified cartilage and surrounded by osteoid tissue. Adjacent to the concave surface of this spicule a few giant cells can be seen. In many places the surface of the cartilage is covered with a layer of osteoblasts. In all parts of the section the marrow has been replaced by fibrous tissue.

obtained from the midportion of the anterior aspect of the right femur; the bone of the femur was soft and was penetrated easily by a curet. The marrow was found to be abundant and highly vascular. A stained smear of the blood which oozed from the marrow cavity failed to yield useful information. Several fragments of bone

were obtained for microscopic examination; none measured more than a few millimeters in any dimension. On gross inspection they were found to be composed of soft pieces of calcified bone, gray cartilage and bright red marrow. Histologic section of the specimen (fig. 16) showed numerous imperfect trabeculae, which were composed of osteoid tissue or of bone surrounded by osteoid tissue. A moderate number of osteoblasts were present about the trabeculae. Few osteoclasts were seen except at the periphery of a mass of hyaline cartilage which was present in several of the sections. Islands of calcium were encountered in the cartilage and in the osteoid tissue which surrounded it; the surface of the cartilage was covered with osteoid tissue. The marrow was replaced by dense collagenous connective tissue which contained numerous multinucleated giant cells and some yellowish brown pigment lying between the connective tissue cells. Normal marrow was not found. The cortical bone was thin and irregular but, even in the demineralized specimens, appeared to contain an abundance of calcium. The haversian canals of the cortex were wide and filled with fibrous connective tissue. No foam cells or cholesterol deposits were found in any of the material which was examined histologically. Mosaic structure was not apparent.

A second specimen was obtained from the extensor surface of the left ulna at a point about 5 cm. from the olecranon. The cortex of the bone was extraordinarily hard: Great difficulty was experienced in removing a piece of bone, and the edges of two chisels were dulled in the process. In contrast with that of the femur, the marrow was avascular. A rectangular piece of bone was removed, measuring 6 by 4 by 2 mm. Microscopic examination of sections made of this material after decalcification revealed that it was composed of normal-looking cortical bone. A small amount of cellular marrow was attached to the internal surface.

The anatomic diagnosis was osteitis fibrosa.

During June 1933, when the child was almost 7 years old, Dr. Raphael Kurzrok, of the Sloane Hospital for Women, measured the daily excretion of estrogenic and gonadotropic substances in ten serial twenty-four hour specimens of urine; the first voiding in the morning was collected separately. On all but three days, when the tests yielded negative results, the child excreted more than 4 rat units daily of estrogenic substance, an amount, in Dr. Kurzrok's opinion, equal to the daily urinary output of an adult woman. Gonadotropic substance was absent from all specimens save one, in which it appeared in high concentration. This specimen was obtained seventeen days after the onset of the last menstrual period and ten days before the appearance of the next. The sudden, explosive output of gonadotropic substance was thought to represent the occurrence of ovulation.

In May 1396, when the child was 9 years and 8 months of age, two twenty-four hour specimens of urine were examined for estrogen. One specimen contained more than 16 rat units per liter of urine; the other, more than 96 rat units. The presence or absence of gonadotropic substance was not determined.

In December 1936, when the patient was 10 years and 3 months of age, several good-sized fragments of bone were obtained at an elective operation on the right mastoid. Fresh preparations of this bone were examined with the polarizing microscope both at room temperature and after warming. Neither doubly refractile particles nor foam cells were identified.

Histologic examination of a small piece of skin removed from the region of the right internal malleolus revealed the presence of a considerable quantity of granular brown pigment which resembled melanin. The pigment was concentrated within the cells of the basal layer of the epidermis, although in some places it was found within the cells of the stratum germinativum. Hypertrophied nerve fibers were not evident.

A tolerance test with 1.75 Gm. of dextrose per kilogram of body weight (22.7 Kg.) ingested by mouth gave the following values for the blood sugar content: after fasting, 85 mg. per hundred cubic centimeters; one hour after the administration of dextrose, 214 mg.; two hours after, 106 mg.; three hours after, 106 mg.; four hours after, 78 mg.; five hours after, 77 mg. During the first, second and third hours dextrose appeared in the urine in concentrations designated ++ and ++++.

During a short study made while the patient was receiving an ample diet, she excreted 0.4 Gm. of creatinine and 0.48 Gm. of creatine in twenty-four hours. The creatinine coefficient was 6.6 mg. Of 1 Gm. of creatine administered by mouth, 31 per cent was excreted as creatine during the first twenty-four hours and 8 per cent during the next twenty-four hours.

Efforts at Therapy.—During the five years which have elapsed since the patient came under our care she has received a "high-calcium" diet with fair consistency; her daily consumption of milk has amounted to between 1,000 cc. and 1,500 cc. Vitamin D has been administered periodically in doses which have varied from 1,000 to 10,000 U. S. P. units daily. In December 1935, when she was 9 years and 3 months old, a short series of roentgen treatments was applied over the thyroid gland and over the midportion of the right femur. All treatment has proved fruitless. The parents have been unwilling to permit thyroidectomy or exploratory laparotomy.

INFORMATION RELATING TO SIMILAR CASES

That the syndrome which the child presents is exceedingly rare is demonstrated by the fact that of the numerous American and European physicians who examined her when she was between 5 and 8 years of age none were able to recall having seen a similar patient. We are indebted to Dr. A. B. Gutman, of the department of medicine of this university, for calling to our attention the first patient with an identical condition [15] of whom we heard and to Dr. Robert Jennings, who told us of a patient [16] whom he saw while an intern in the Children's Hospital, Boston.

In 1922 Weil [17] presented the case of a 9 year old girl before a medical assembly in Breslau.

The child's sexual and skeletal development was equal to that of a girl 15 years of age. She had menstruated since infancy and had suffered seven spontaneous fractures, the first of which occurred when she was 18 months old. The skin was abnormally pigmented, and the scleras were slightly blue. Weil expressed

15. Goldhamer, K.: Osteodystrophia fibrosa unilateralis (kombiniert mit Pubertas praecox und mit gleichseitigen osteosklerotischen Veränderungen des Schädels), Fortschr. a. d. Geb. d. Röntgenstrahlen **49**:456, 1934. Preliminary reports of this case will be found in Offizielles Protokoll der Gesellschaft der Aerzte in Wien. Salzer, H.: Wien. klin. Wchnschr. **46**:862, 1933. Goldhamer, K.: ibid. **47**:218, 1934.

16. (*a*) Transactions of the Society for Pediatric Research, Annual Meeting, May 5, 1936, Am. J. Dis. Child. **52**:743 (Sept.) 1936. (*b*) Freedman, H. J.: Disturbances of Function of the Suprarenal Glands in Children, ibid. **44**:1285 (Dec.) 1932.

17. Weil: Medizinische Sektion der Schlesischen Gesellschaft für vaterländische Kultur zu Breslau, Klin. Wchnschr. **1**:2114, 1922.

the opinion that the precocious sexual development was related to abnormality of the suprarenal glands. The roentgenographic appearance of the bones suggested that the patient had an unusual variety of osteopsathyrosis.

In 1932 Gaupp reported two cases from Germany.[18] Both patients were white girls who exhibited premature puberty and an unusual type of generalized fibrocystic disease of the skeleton. In one case abnormal pigmentation was present, and in the other the presence or absence of pigmentation was not mentioned.

The first patient was 8 years old, the only child of healthy parents. Birth had occurred spontaneously, although delivery had been difficult. The weight at birth was 2,200 Gm. (4.8 pounds). Dentition proceeded normally. Although the child learned to walk and to talk at the usual time, she was regarded as a delicate infant. At the age of 2 years she complained of pain in both lower extremities and began to limp, dragging the right foot. At 3 years the breasts commenced to enlarge, hair appeared in the axillary and public regions and the child began to menstruate. During the ensuing five years she suffered numerous pathologic fractures of the proximal and the distal portion of the left leg; the bones healed promptly. Throughout this period the lower extremities became progressively deformed. The menses continued to appear regularly at intervals of eight weeks and lasted one or two days. At the age of 8 years the patient's secondary sex characters were those of an immature adult woman. The blood pressure was normal. Roentgen examination revealed the presence of a diffuse lesion of the skeleton which involved the pelvis and all four extremities, including the small bones of the hands. The ribs were not demonstrably affected, and the skull appeared normal. The outstanding roentgenographic feature was coarse-grained osteoporosis associated with numerous small cysts. In some places the cortex appeared to have been destroyed, and in others the periosteum was thickened. Osteotomy was undertaken for therapeutic reasons. At operation the periosteum was found to be thick and vascular; the bones were soft and could be cut with a knife; the cortex was thin, and the subcortical bone was spongy. Fragments of bone removed at operation exihibited histologically "a picture typical of osteitis fibrosa"; i. e., there were spongy trabeculae which lacked clearcut lamellation; the marrow which occupied the intertrabecular spaces was fibrous, and the cortical bone was defective. Numerous osteoblasts were found, as well as a moderate amount of osteoid tissue; however, the scarcity of osteoclasts was striking.

The serum calcium content was in the neighborhood of 11 mg. per hundred cubic centimeters on several occasions. Metabolism studies (which are not reported in detail in the paper from which this information was culled) when the child was 7 years old and again when she was 8 revealed normal excretion of calcium in the urine. During the first study between 0.04 and 0.123 Gm. appeared in the urine daily, and during the second study the urinary calcium was "normal." The patient was treated unsuccessfully with glandular extracts and with preparations of vitamin D. Surgical exploration of the neck at the age of 8 years revealed two normal parathyroid bodies; others were not encountered. A small nodule, which was later found to be composed of thyroid tissue, was extirpated. In addition, about one third of a normal parathyroid gland was removed, and both

18. Gaupp, V.: Pubertas praecox bei Osteodystrophia fibrosa. Monatschr. f. Kinderh. **53**:312, 1932.

inferior thyroid arteries were ligated. Nine months later the patient was definitely better, although the roentgenographic features of the skeleton remained unchanged. The outcome of the therapy could not be predicted at the time of the report. The author did not state whether or not this patient's skin was pigmented. The photograph which was reproduced showed no abnormalities of the skin of the front of the body.

Gaupp's second patient was a 9 year old girl born of healthy parents. Two sisters died in infancy of diarrheal disease, and one sister was well. The patient was born normally at term, weighing 2,000 Gm. (4.4 pounds). Although her health was poor during infancy and early childhood, she walked at the age of 1 year and talked at 16 months. Rickets developed during the second year of life. During this period she had chickenpox and whooping cough. She contracted measles and scarlet fever at the age of 6 years. Between her first and her second birthday the child's gait assumed a waddling character; shortly afterward she complained of pain in the right leg. By the time she was 6 years old the thighs were markedly bowed. Although the occurrence of pathologic fractures was not recognized before the sixth year, numerous fractures took place thereafter. Manifestations of pubescence appeared early in life, and menstruation began at 9 years. At this age the child exhibited the mammary and genital development of an adolescent girl, as well as the corresponding development of axillary and pubic hair. She was 137 cm. (55 inches) in height and well nourished. A pigmented mole the size of the palm of the hand was present on the left buttock. Her head appeared somewhat large and rectangular. Slight bilateral exophthalmos was present, together with a moderate-sized struma. Other signs of hyperthyroidism were absent. The spine was kyphotic and the femurs bowed; the right leg was 2 cm. shorter than the left, and the mobility of the hip joint was diminished. Roentgenographically, the bones showed "honeycomb" osteoporosis and numerous small cysts and the skull appeared normal. The microscopic features of a fragment of bone which was removed from the right femur were "typical of osteodystrophy." The serum calcium content was "normal." A balance study of the calcium metabolism, the details of which were not published, yielded "normal" results. The neck was explored surgically, but no parathyroid tissue was identified. The patient was treated fruitlessly with a preparation of the anterior lobe of the hypophysis. By the time she was 11 years old the inconspicuous evidence of hyperthyroidism which had been present earlier had disappeared. However, serial roentgenograms revealed uninterrupted progression of the skeletal lesions, and several new pathologic fractures had occurred.

In 1932 Freedman [16b] reported the case of an infant of Italian stock who became a patient of the Boston Dispensary at the age of 6 months because of celiac disease.

The infant had begun to menstruate two months before. At 6 months she showed a moderate amount of brownish pigmentation of the skin of the face, the left leg and the left buttock and well marked evidence of precocious puberty. Slight hypertension was present. The Aschheim-Zondek test failed to reveal an abnormal quantity of gonadotropic substance in the urine. The infant continued to menstruate regularly up to the age of 14 months, when the report was submitted. The pigmented areas of the skin had increased in number and size, and the color had become deeper.

Dr. Alan M. Butler supplied the details of the patient's subsequent course.[16]

She was studied in the Children's Hospital, Boston, at the age of 3 years and again at 6 years. She entered the institution at 3 years because of a pathologic fracture of the left femur. She was found to be mentally retarded. The skin showed numerous patches of brown pigmentation. Precocious puberty was well established. Chemical studies of the blood yielded normal results: The calcium content of the serum was 9.7 mg. per hundred cubic centimeters and the inorganic phosphorus content 4.1 mg.; the cholesterol content of the plasma was 114 mg., and the sodium content of the serum was 133 milliequivalents per liter and the chloride content 100 milliequivalents. The plasma phosphatase activity was 1.5 Kay units. The urine contained neither gonadotropic nor estrogenic substance. An intravenous urogram yielded normal results. Spinal encephalography demonstrated slight internal hydrocephalus and moderate cerebral defect. Roentgenographic examination of the skeleton revealed the presence of pathologic features similar to those which have been described in the report of our patient; however, the lesions were distributed symmetrically and were equally severe on the two sides. When the child was 3 years of age the development of the bones of the carpi was that of a 7 year old child. Surgical exploration of the abdomen failed to reveal evidence of adrenal tumor. A benign cyst was removed from one ovary, but this did not subsequently affect the patient's condition.

Roentgen treatment of the pituitary gland proved fruitless. The child continued to menstruate regularly and suffered further pathologic fractures. Examination when she was approximately 6 years old revealed progression of the skeletal lesions. The chemical aspects of the blood had remained normal. At this time the urine contained a trace of Bence-Jones' protein but neither estrogenic nor gonadotropic substance.

The following brief report of what we regard to be a case in point appeared in a paper on the pathogenesis of von Recklinghausen's neurofibromatosis, published by Stalmann in 1933.[19] A translation of his description follows:

"3. K. G., 8 years old. The family history was irrelevant. The child's skin exhibited pigmented patches at birth. The menses appeared when the child was 9 months old and have been regular since she was 2 years old. When she was 5, osteitis fibrosa developed, with gradual bowing of the femurs, first of the right and later of the left. Spontaneous fractures have occurred.

"Physical Examination: The child is of moderate stature (130 cm.). Evidence of precocious puberty is present; menstruation, pubic hair, slight hypertrophy of the breasts. The skin exhibits widespread patches of dark brown pigment; these are not arranged segmentally. The patches are somewhat striped. There is an exostosis at the margin of the right orbit. The spine is scoliotic, with the convexity to the right. Coxa vara is present on both sides. The thighs are bowed into the shape of the letter 'O.' The intellect is normal, the emotions repressed and the personality reserved. Roentgen examination reveals severe osteitis fibrosa cystica of the right femur.

19. Stalmann, A.: Nerven-, Haut- und Knochenveränderungen bei der Neurofibromatosis Recklinghausen und ihre entstehungsgeschichtlichen Zusammenhänge, Virchows Arch. f. path. Anat. **289**:96, 1933.

"Subsequently, the patient suffered numerous spontaneous fractures; all healed promptly."

The most comprehensive report of a case in which the condition was apparently identical with ours was published by Goldhamer, of Vienna, Austria, in 1934.[15]

The patient was a 9 year old white girl, the only child of healthy parents. She menstruated irregularly from the age of 2 years. A bony tumor appeared in the region of the left mandible when she was 3 years old. At this time the child complained of pain in the left thigh. At 5 years she sustained a pathologic fracture of the left femur. When she was 7 years old menstruation was well established and regular; the breasts and the external genitals had developed to a degree equal to that of a much older person. At the age of 10 years the patient was described as a large, thin and somewhat pale child. A large brown nevus was present on the neck and another over the sacrum. The teeth were carious. The thyroid was not enlarged. Slight exophthalmos, which was bilateral but asymmetrical, was present. There was moderate atrophy of the left hip and left leg, accompanied by curvature of the femur on the same side. A hard tumor, which seemed to be attached to bone, could be felt in the region of the left trochanter. Fusiform swelling was present in the left mandible. The serum calcium content was 11.4 mg. per hundred cubic centimeters. The systolic blood pressure was 125 mm. of mercury and the diastolic 75 mm. When the child was 12 years old the concentration of calcium in the serum was 12.2 mg. per hundred cubic centimeters, and that of inorganic phosphorus was 5 mg. At this time 0.132 Gm. of calcium was found in a nineteen-hour specimen of urine (29.4 mg. per hundred cubic centimeters); a twenty-four-hour specimen of urine contained 0.168 Gm. of inorganic phosphorus and 0.29 Gm. of total phosphorus. A few months later the calcium content of the serum was found to be 12 mg. per hundred cubic centimeters and the inorganic phosphorus 2.7 mg. The concentration of calcium in the urine was 12.3 mg. per hundred cubic centimeters and that of phosphorus 1.18 Gm. (P_2O_5 2.71 Gm.) per liter. The serum cholesterol content was normal. The skeleton was examined roentgenographically several times when the patient was between 4 and 5 years old. A mixture of sclerosing, porotic and cystic lesions was found; these were limited sharply to the left half of the skeleton but involved all the bones on the affected side. The child's skeletal age was estimated to be about 15 years.

A specimen of bone was removed from the region of one of the cystlike areas in the left femur. Although it contained a small amount of mature trabecular bone, it consisted chiefly of poorly differentiated, calcified spicules, many of which were enclosed in a rim of osteoid tissue. The spaces between the spicules were filled with highly cellular fibrous tissue. Giant cells were not found; however, numerous spherical cells were encountered, the cytoplasm of which was packed with hemosiderin, presumably the result of previous hemorrhage.

During the time the child was under observation she sustained a pathologic fracture of the proximal portion of the left femur. Goldhamer did not enumerate the therapeutic efforts which were made in this case.

When the record of our patient was presented before the Society for Pediatric Research, in May 1936,[16a] Dr. Fuller Albright, of Boston, recounted having seen two patients who presented similar clinical features.

The first was a 23 year old woman one half of whose skeleton exhibited cysts; she had begun to menstruate at the age of 7 years. The second patient was a woman of 40 years whose bones, also, were cystic. In her case menstruation had commenced at the age of 1 year and longitudinal growth had ceased at 10 years. Despite these difficulties, the woman had married and had borne children. Both patients exhibited pathologic pigmentation of the skin. In both cases balance experiments and chemical studies of the blood had yielded no evidence of abnormal calcium metabolism.

Dr. Albright also alluded to another case which he had heard of, that of an 8 year old girl who exhibited the combination of premature puberty, abnormal pigmentation of the skin and skeletal changes suggestive of osteitis fibrosa cystica.

Finally, Dr. Albright called attention to a case of Snapper and Parisel [20] which, if the condition can be shown to be identical with that in the other cases included in this series, possesses great importance.

The patient was a mentally defective girl who began to menstruate when she was 7 years old. Between the ages of 7 and 9 years she suffered five pathologic fractures involving both femurs; after this an interval occurred during which no more fractures took place. At the age of 10 years a general examination failed to show "anything abnormal." The Wassermann reaction was negative. The basal metabolic rate was normal. The serum calcium content was 12.6 mg. per hundred cubic centimeters. Several small brown nevi were present on the face and the chest. The proximal portions of both thighs were grossly deformed; one of the legs was shorter than the other, and the right humerus was swollen. Roentgenographic examination showed that both femurs and many other bones of the skeleton were markedly and homogeneously osteoporotic and that many cysts were present throughout the skeleton. The righ humerus was most severely affected. The skull was normal. Two surgical explorations of the neck resulted in failure to find a parathyroid tumor. Profiting by the experience of Kienböck and Meworach,[21] the authors resorted to biopsy of the subtrochanteric region of the femur. The tissue which was removed showed histologic features indistinguishable from those of osteitis fibrosa cystica. In addition, a considerable number of cholesterol-laden foam cells were found; this feature suggested a diagnosis of xanthomatosis ossium. Although the patient's serum cholesterol content had been as high as 322 mg. per hundred cubic centimeters during an earlier period of the illness, it did not rise above 197 mg. during the time she was under the authors' observation.

The common features of the foregoing cases are: precocious puberty, an unidentified variety of pathologic pigmentation of the skin and a type of systemic disease of the skeleton which may be designated descriptively as osteodystrophia fibrosa.

In examining the pertinent literature, we found that a small number of male patients have exhibited a similar type of osteodystrophy and

20. Snapper, I., and Parisel, C.: Xanthomatosis Generalisata Ossium, Quart. J. Med. **2**:407, 1933.

21. Kienböck, R., and Meworach, L.: Ein Fall von multiplen Xanthomen in den Knochen, Röntgenpraxis **4**:76, 1932.

like pigmentation of the skin. So far as can be determined, none of these patients showed accelerated physical development or pubertal precocity. The clinical and pathologic relationship of their condition to that described in the foregoing section is speculative. We summarize their cases as briefly as possible.

Two cases of this sort were reported by Priesel and Wagner.[22]

The first patient was a 13 year old boy who had enjoyed good health, except for repeated nosebleeds, until the age of 11 years. After a febrile illness at that time he complained of pain in the right hip and began to limp, and during the next two years he found it increasingly difficult to walk. When he came to the attention of the authors, at the age of 13 years, the right thigh was bowed and the right leg shorter than the left. A large pigmented nevus was present on the right buttock. Roentgenographic examination revealed that the right femur, tibia, fibula, ilium and humerus, as well as the left tibia and fibula, were affected by a lesion which was characterized by metamorphosis (*Umbau*) of the structure of the bone. The delicate tracery of the spongiosa was replaced by coarse shadows interspersed with numerous areas of diminished density, which bore the appearance of cysts; the bones were expanded, and some of them were curved; thinning and fracture of the cortex were present in many locations. The skull was normal. The calcium content of the serum varied between 9.8 mg. and 13.6 mg. per hundred cubic centimeters during the first four months of medical observation, and the inorganic phosphorus, between 4.4 and 4.8 mg. During this period the urinary calcium was measured on five occasions; it varied between 0.144 Gm. and 0.290 Gm. (presumably in twenty-four hours). A preparation of vitamin D[23] was employed for one month in doses of 10 mg. daily, without demonstrable benefit to the patient. The removal of a single microscopically normal parathyroid gland failed to effect improvement. During the five months which followed operation the calcium content of the urine was determined several times to be between 0.357 Gm. and 0.147 Gm. (presumably in twenty-four hours). The calcium content of the serum fluctuated between 11.6 mg. and 16.0 mg., and the inorganic phosphorus content remained normal. Eight months after operation the concentration of calcium in the serum was 10.8 mg. Neither clinical nor roentgenographic improvement had occurred, and the right lower extremity exhibited progressive deformity.

The second patient was a 7 year old boy who also had had severe and frequent nosebleeds; in addition, he had had one severe hemorrhage after the extraction of a tooth. Suddenly, at the age of 7 years, he complained of pain in both thighs, had difficulty in walking and began to limp. At this time he was found to have a large, dark, pigmented nevus on the back and a lighter colored one on the neck. The scleras were bluish. The cutaneous vessels were abnormally fragile. The bleeding time was five mintues and the clotting time seven minutes. The blood platelets numbered 374,000 per cubic millimeter. Roentgenographic examination revealed the presence of generalized fibrocystic disease of the skeleton. Although well marked changes were present in all the bones of the upper extremity, including those of the hands, the left femur was most severely affected. Only the right

22. Priesel, R., and Wagner, R.: Ostitis fibrosa cystica generalisata (Osteodystrophia fibrosa), Ztschr. f. Kinderh. **53**:146, 1932. A preliminary report of these cases appeared in the Transactions of the Second International Pediatric Congress, Stockholm, 1930, Acta pædiat. **11**:237, 1930.

23. The preparation used was vigantol.

radius and both tibias and fibulas were spared. During a six month period of medical study the calcium content of the serum varied between 10.2 and 22.8 mg. per hundred cubic centimeters and the inorganic phosphorus content remained stable at about 6 mg. The excretion of calcium in the urine was found to vary between 0.264 and 0.050 Gm. (presumably in twenty-four hours). The child was treated with various antirachitic substances and with calcium for four months; he regained his ability to walk and could even jump. However, he suffered a pathologic fracture of the left femur two months after treatment was discontinued.

The history of the sexual development of these patients was not described. It was stated that the external genitals of the first child (13 years old) were "childish." Biopsy of bone was not performed.

Hummel [24] reported two similar cases in 1934.

One boy was 11 and the other 9½ years old. Both patients had suffered numerous pathologic fractures, which were due to extensive fibrocystic disease of the skeleton. When they were examined both boys exhibited patches of pigmentation of the skin and the deformities which had resulted from degeneration of the skeleton and from the fractures. Histologic examination was made twice in the case of the first patient. When he was 7 years old, the specimen examined was found to consist of spongy bone which displayed evidence of active destruction and regeneration, and some of the trabeculae exhibited what Schmorl has designated mosaic structure. The marrow was fibrous. When he was 11, similar evidence of active tissue metabolism was present in both the cortical and the spongy portions of the bone, mosaic structure was again indentified and the marrow was still fibrous. In portions of the specimen, large spaces were present; some of these were lined by osteoid tissue and others by osteoblasts. Microscopic studies were not made in the other case. In neither case was the degree of sexual maturity commented on. Chemical studies of the blood and the urine were not made. The photographs reproduced showed that the pigmentation of the first patient bears a striking visual resemblance to that of our patient.

Finally, we wish to mention the case reported by Hirsch [25] in 1929.

The patient has been studied recently in the Presbyterian Hospital, New York.[26] This person, who is now over 30 years of age, exhibits pathologic pigmentation of the skin which is identical in character with that of our patient but which is confined to the lower extremities. The roentgenographic appearance of the skull is characteristic of Paget's disease, while that of the rest of the skeleton is typical of osteitis fibrosa cystica. During many years of close medical observation, the serum calcium content has never been determined to be elevated. Although he was shown at one time to be in negative mineral balance, excretion of calcium in the urine was not increased. The plasma phosphatase activity has been consistently greater than normal. Microscopic examination of fragments of bone removed from the sternum revealed features compatible with osteitis

24. Hummel, R.: Zwei Fälle von Ostitis deformans Paget juvenilis, Röntgenpraxis **6**:513, 1934.

25. Hirsch, I. S.: Is Generalized Osteitis Fibrosa (Paget and von Recklinghausen) Congenital? Am. J. Surg. **3**:167, 1927; Generalized Osteitis Fibrosa, Radiology **13**:44 (July) 1929.

26. Gutman, A. B.; Swenson, P. C., and Parsons, W. B.: The Differential Diagnosis of Hyperparathyroidism, J. A. M. A. **103**:87 (July 14) 1934.

fibrosa cystica. Extensive surgical exploration of the neck, on two occasions, failed to reveal tumor of the parathyroid bodies. The patient was not demonstrably benefited by the removal of one normal parathyroid gland.

In none of the foregoing cases, in either males or females, has the outcome been fatal. Although it may be surmised that patients with conditions of this sort have come to autopsy, we have not encountered any reports.

COMMENT

The reader was warned in the beginning that we have not been able to formulate a comprehensive and conclusive solution of the diagnostic problem presented by the patient reported on in this paper. With reference to classification, presumably she belongs to the group composed of the female patients of Weil, Gaupp, Freedman and Butler, Stalmann, Goldhamer and Albright and possibly the patient of Snapper and Parisel.[27] The relation of this group to that which comprises the male patients of Priesel and Wagner and Hummel and that of Hirsch and Gutman is suppositional. The ability to classify the patient, although an unsatisfactory substitute for a neat and objectively grounded explanation for the condition, is not entirely without value. In the first place, it demonstrates that the syndrome is not unique. This is a point of some importance, since it suggests, although it does not prove, that the precocious puberty, the osseous dystrophy and the pigmentation are associated, not solely as a matter of chance, but because of some common causal factor. In the second place, the information derived from the other cases can be used to supplement or to confirm our findings and to assist in analyzing them critically.

What, then, is the feature common to all the cases of the two groups under discussion? In the quest for conditions similar to ours we sought principally examples of diffuse osteitis associated with precocious puberty or with pigmentation of the skin or with both. For this reason, generalized osteitis is the one feature shared by all the patients described in the foregoing section. In the majority of the cases the whole skeleton was compromised, although not all the bones were affected with equal severity. In Goldhamer's case the lesion was strikingly unilateral—so one sided, in fact, that only half of the skull was involved. In our own case, although the entire skeleton was invaded progressively, the lesions appeared earlier and were more severe on the right side than on the left. In all the cases the outstanding roentgenographic feature was the presence of a mixture of both diffuse and cystlike osteoporosis;

27. We have examined the details of the case of a 7 year old girl reported by Ernst Freund under the title "Osteodystrophia Fibrosa Unilateralis" (Arch. Surg. **28**:849 [May] 1934). The child's skin was not characterized by pathologic pigmentation and, according to a personal communication from Dr. Freund to the authors, she did not exhibit precocious puberty.

this was frequently accompanied by areas of sclerosis in various parts of the skeleton, by alteration of the normal contour of the bones and by evidence of pathologic fracture. The female patients, all of whom exhibited precocious puberty, showed accelerated maturation of the skeleton. In this respect they differed from the male patients, whose sexual and skeletal development was congruous with their chronological age. With two outstanding exceptions, microscopic examination revealed considerable similarity in the histologic features of the bones. These features consisted principally of a disorderly combination of poorly differentiated bone, calcified and uncalcified osteoid tissue and fibrous marrow. Osteoblasts were usually observed in the normal number. A relative scarcity of osteoclasts was evident in Goldhamer's case and in our own. In addition to this uniform pattern, Hummel found clearcut features of the mosaic structure which Schmorl [28] regarded as an important histologic criterion of Paget's disease. Although Snapper and Parisel observed the nonspecific changes of osteitis fibrosa, they also found foam cells which contained a sudan-staining lipoid material the doubly refractile property of which suggested that it was cholesterol.

The chemical data which relate to the cause of the osseous disturbance are somewhat contradictory. In the cases of Gaupp, Freedman and Butler, Albright, Hirsch and Gutman and in our case the calcium and the inorganic phosphorus content of the serum were consistently normal. Snapper and Parisel reported the calcium content to be slightly elevated (12.6 mg. per hundred cubic centimeters) on one occasion; the inorganic phosphorus content was not measured. In Goldhamer's case the calcium content was somewhat increased (12.2 and 12 mg.). One determination showed the inorganic phosphorus content to be normal (5 mg.), and at another time it was decreased (2.7 mg.). On the other hand, both patients of Priesel and Wagner displayed marked hypercalcemia. This finding may indicate a fundamental difference between the condition in these two cases and that in the others which are under discussion. However, the fact that the serum calcium content may be strikingly elevated in cases of leukemic myelosis [29] robs hypercalcemia of some of the specific significance which it was formerly thought to possess with reference to the diagnosis of primary hyperparathyroidism. Balance studies of the calcium metabolism gave normal results in both of Gaupp's cases and also, we understand,[16] in Albright's.

28. Schmorl, G.: Ueber Ostitis deformans Paget, Virchows Arch. f. path. Anat. **283**: 694, 1932.

29. Duken, J.: Beitrag zur Kenntnis der malacischen Erkrankungen des kindlichen Skelettsystems: I. Mitteilung, Spätrachitis und Osteodystrophia fibrosa, Ztschr. f. Kinderh. **46**:114, 1928. We have recently seen a patient with a similar condition, a 3 year old girl with extensive leukemic involvement of the skeleton. The serum calcium content rose as high as 17.6 mg. per hundred cubic centimeters.

Our patient was shown to be in positive balance for calcium and phosphorus on two occasions and to have a normal twenty-four-hour amount of urinary calcium during a third study; she has never shown hypercalciuria. The data relating to the excretion of calcium and phosphorus in the urine of Goldhamer's patient are scanty and difficult to interpret, but they suggest that the urinary calcium and phosphorus were increased. Both patients of Priesel and Wagner excreted abnormally large amounts of calcium and phosphorus in their urine. This finding is not surprising in view of the hypercalcemia already mentioned. Although in negative mineral balance when studied in the Presbyterian Hospital, the patient of Hirsch and Gutman did not show hypercalciuria.[26] The plasma phosphatase activity was normal on two occasions in the case of Freedman and Butler; on the other hand, it was found to be elevated in the case of Hirsch and Gutman and in our own. The significance of this incongruity is not certain. The concentration of gonadotropic substance in the blood of our patient was normal. This measurement was not employed in the other cases. The neck was explored surgically once in both of Gaupp's cases, in one of the cases of Priesel and Wagner and in ours; two explorations were made in the case of Hirsch and Gutman and two in the case of Snapper and Parisel. In no case was tumor of the parathyroid glands observed. The general health of one of Gaupp's patients improved temporarily after a fragment of normal parathyroid tissue had been removed; however, the roentgenographic appearance of the bones was unchanged several months later. Removal of normal parathyroid tissue failed to help the patient of Priesel and Wagner or that of Hirsch and Gutman. None of the patients have shown kidney stone or manifestations of impairment of renal function.

The evidence accumulated from these cases argues strongly against the possibility that the cause of the osseous disturbance is to be found in classic hyperparathyroidism—that is, in hyperparathyroidism associated with adenomatous enlargement of one of the glands and characterized by demonstrable and typical disturbance in the metabolism of the calcium and phosphorus. Parathyroid hyperfunction of an intermittent or of a highly subtle nature, without tumefaction of one of the glands, cannot be excluded categorically. The unilateral distribution of the lesions in Goldhamer's case and their one-sided predominance in our patient constitute a strong argument that the changes in the bones are not wholly or immediately of endocrine origin. In concluding this portion of the discussion, we wish to add that cases of proved "primary" hyperparathyroidism, that is, of hyperparathyroidism which is not related to hypovitaminotic [11] or to renal [12] rickets, have not been reported in children. Whether our patient was a child in the developmental sense of the word when the disturbances of the skeleton first

made their appearance is, admittedly, a point concerning which the incomplete character of the early history does not permit us to decide.

One of the common causes of severe deformity of the skeleton in children is chondrodysplasia. Several clinical varieties of this anomaly of development have been described, e. g., achondroplastic dwarfism, multiple cartilaginous exostoses (hereditary deforming chondrodysplasia) and Ollier's disease. The term Ollier's disease [30] refers to a clinical type of chondrodysplasia in which one half of the skeleton is affected exclusively or at least more extensively than the other. The roentgenographic appearance of certain portions of our patient's skeleton is not unlike that observed in chondrodysplasia, notably, that of the distal portion of the right ulna (fig. 11) and the distal end of the right femur (fig. 7). In addition, a considerable amount of cartilage was found in the fragments of bone removed from the right femur (fig. 16). However, the intact state of the epiphysial lines throughout the greater part of the skeleton, as well as the general results of the histologic examination, in our case and in the other cases provide strong evidence that the skeletal changes are not due to chondrodysplasia. Dr. A. M. Pappenheimer, who examined the sections obtained from our patient, was inclined to regard the presence of cartilage as the result of the numerous fractures which had taken place in the right femur.

Although Gutman and Kasabach [31] stated that no case of authentic Paget's disease had been recognized in persons under the age of 25, they conceded that the early manifestations of osteitis deformans are so insidious that few patients can date the onset of their illness. Since, from the point of view of vulnerability to disease, the female patients of this series are to be regarded as young adults, it is conceivable that they might have Paget's disease. Furthermore, a number of cases have been described in children in which the term "Paget-like" changes has been used, correctly or incorrectly, to describe the roentgenographic features of the bones. As examples, we cite the case of Ivimey [32] and that of Jundell and Vilén.[33] Finally, if it is true that the disease of the skeleton of one of Hummel's patients is identical with that presented by our patient, the presence of "mosaic structure" in the bones may have an important bearing on the diagnosis in our case. We have had no personal experience with cases of proved osteitis deformans. We are indebted to several roentgenologists who have examined the films of our

30. Cole, W. H.: Chondrodysplasia, Surg., Gynec. & Obst. **42**:359, 1926.

31. Gutman, A. B., and Kasabach, H.: Paget's Disease (Osteitis Deformans), Am. J. M. Sc. **191**:361, 1936.

32. Ivimey, M.: Bone Dystrophy with Characteristics of Leontiasis Ossea, Osteitis Deformans and Osteitis Fibrosa Cystica in a Child, Am. J. Dis. Child. **38**:348 (Aug.) 1929.

33. Jundell, I., and Vilén, A.: Ein Beitrag zur Kenntnis der Leontiasis ossea, Acta pædiat. **15**:438, 1934.

patient for the opinion that, although certain aspects of the skeleton are compatible with those in Paget's disease, the predominant lesions are of another character.

Multiple xanthomatosis is a well known cause of destructive lesions of the skeleton.[34] Six children with xanthomatosis ossium have been treated in this institution within the last few years. From time to time the possibility has been entertained that our patient might have xanthomatosis. Dr. R. S. Rowland, whose experience in this field entitles his judgment to especial authority,[35] once expressed the opinion that the appearance of our patient's skeleton was not unlike that observed in certain cases of xanthomatosis ossium. Dr. Albright [16] has implied that he regards the condition reported by Snapper and Parisel as cholesterosis of the skeleton to be identical with the condition in his own cases, in the case of Freedman and Butler and in ours. Calling attention to the structural similarity which exists between cholesterol and the estrogenic substances,[36] he offered the highly stimulating speculation that the relation between ths osseous dystrophy and the precocious puberty in these patients might be found in a disturbance of the metabolism of the lipoid substances.

The resemblance of the patient of Snapper and Parisel to the patients under discussion cannot be denied, although puberty appeared later (at the age of 7 years) and the pigmentary anomalies were less conspicuous than in many of the other patients. We are not in complete agreement with Dr. Albright that the features of the roentgenograms which Snapper and Parisel reproduced are exactly like those in our case; however, it is probably unimaginative to expect the protean pathologic processes which operate in generalized xanthomatosis always to produce lesions in the skeleton which will be strictly comparable roentgenographically. The histologic characters of xanthomatosis ossium are extremely variable.[37] They consist of the specific features produced by the presence of lipoid material and the nonspecific alterations due to destruction and repair of bone. For this reason, microscopic examination of fragmentary material from a few regions of the skeleton might easily fail to supply definitive diagnostic information. None of the histologic examinations which we have summarized revealed features

34. Merritt, K. K., and Paige, B. H.: Xanthomatosis (Schüller-Christian Syndrome), Am. J. Dis. Child. **46**:1368 (Dec.) 1933.

35. Rowland, R. S.: Anomalies of Lipid Metabolism, in Christian, H. A.: Oxford Medicine, London, Oxford University Press, 1931, vol. 4, chap. VII-A p. 214 (3).

36. Fieser, L. F.: The Chemistry of Natural Products Related to Phenanthrene, Monograph 70, American Chemical Society Series of Scientific and Technologic Monographs, New York, Reinhold Publishing Corporation, 1936.

37. Rowland, R. S.: Schüller-Christian's Disease, Am. J. Roentgenol. **30**: 649, 1933.

which were incompatible with a diagnosis of xanthomatosis ossium, with the possible exception of that in the case of Hummel, in which "mosaic structure" was found. However, if cholesterosis is responsible for the skeletal lesions in all the patients, it is surprising that all the biopsies save that made by Snapper and Parisel should have yielded uniformly negative results in this respect. No evidence of cholesterol deposits was found by Gaupp (two biopsies, two patients), Goldhamer (one biopsy), Hummel (two biopsies on the same patient) or us (three biopsies on the same patient) or in the case of Hirsch and Gutman (one biopsy). In Goldhamer's case the sections showed "spherical cells"; however, these contained hemosiderin, not fat. If the supposition is well grounded that both the female and the male patients whose cases we have collected had the same fundamental disease, it is difficult to conceive the precise nature of a disturbance of the lipoid metabolism which would evoke precocious puberty in females only. A more cogent argument against the xanthomatous origin of the development anomalies lies in the fact that, with the exception of the case of Snapper and Parisel, in none of the large number of cases of xanthomatosis of the skeleton which have been reported has precocious puberty been observed.[38] The endocrine features which have been reported in patients with generalized cholesterosis consist of retarded development and regression rather than physical precocity.[37] On the other hand, the widely disseminated character of the cholesterol deposits in lipoid histiocytosis prepares one to expect almost any type of endocrinopathy. The positive evidence obtained by Snapper and Parisel is impressive; it cannot be disregarded except in the face of equally positive evidence of a contrary nature.

The presence of pathologic pigmentation of the skin in the majority of the patients is a challenging phenomenon. Numerous explanatory possibilities come to mind: hereditary nevi spili, Addison's disease or other functional disturbance of the adrenal glands, Cushing's syndrome and von Recklinghausen's neurofibromatosis. There is no history of similar anomalous pigment in the skin of members of the patients' families. That none of the children had Addison's disease is reasonably evident. Cushing's syndrome can be excluded without difficulty.[39] None of the patients were obese, the females menstruated with considerable regularity, none showed hypertrichosis or alopecia and the abnormalities of pigmentation in both the male and the female patients were entirely different from those which have been described in cases of Cushing's syndrome. We cannot deny the possibility that our patient

38. Personal communications from Dr. R. S. Rowland, Dr. K. K. Merritt and Dr. B. H. Paige.

39. Kessel, F. K.: Morbus Cushing: Ein Ueberblick über Klinik und Kasuistik des basophilen Hypophysenadenoms, Ergebn. d. inn. Med. u. Kinderh. **50**: 620, 1936.

has an adrenal tumor, although this is unlikely. Physical examination has consistently failed to reveal the presence of masses in the region of the kidneys, and roentgenograms have never shown calcification in this region. Neither the diffusely swarthy color of the child's skin nor the geographically outlined nevi resemble the pigmentary changes which occur in association with adrenal tumors. Microscopic examination of a single piece of skin from the right lower extremity yielded information concerning the nature of the pigment (melanin) and its distribution but, as one might expect,[40] failed to provide a clue to the reason for its presence. Excellent descriptions of the cutaneous and osseous manifestations in von Recklinghausen's neurofibromatosis have been published by Brooks and Lehman.[41] Weber has reviewed these aspects, as well as the subject of the endocrine anomalies which have been reported in association with neurofibromatosis.[42] The recent contribution of Stalmann [19] emphasized anew the pleomorphic character of the disease. The paper of Leader and Grand [43] demonstrated convincingly that it is possible to have von Recklinghausen's neurofibromatosis without having cutaneous or subcutaneous neurofibromas. Although it would be possible to contrive an explanation of the triad precocious puberty, osteodystrophy and pigmentation of the skin on the basis of neurofibromatosis, the fact that none of the patients included in this discussion have shown a single cutaneous nodule makes such speculation unsatisfactory. Stalmann did not supply reasons for including his patient in a group with neurofibromatosis.

The precipitating cause of the sexual precocity in our patient and in the female members of the group is entirely unclear. In their extensive review of the subject, to which many subsequent writers refer, Reuben and Manning [44] stated that in most cases of precocious puberty in which the cause of the accelerated development was sufficiently studied the condition was found to be due to functional overactivity or tumorous growth of the pineal gland, the adrenal glands or the gonads. With

40. Meirowsky, E.: Idiotypische Pigmentanomalien, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 4, pt. 2, p. 588.

41. Brooks, B., and Lehman, E. P.: The Bone Changes in Recklinghausen's Neurofibromatosis, Surg., Gynec. & Obst. **38**:587, 1924.

42. Weber, F. Parkes, and Perdrau, J. R.: Periosteal Neurofibromatosis, with a Short Consideration of the Whole Subject of Neurofibromatosis, Quart. J. Med. **23**:151, 1930. Weber, F. Parkes: A Note on Syndromes Sometimes Associated with Retinitis Pigmentosa and Pigmentary Incomplete Forms of Recklinghausen's Disease, M. Press **119**:416, 1925.

43. Leader, S. D., and Grand, M. J. H.: Von Recklinghausen's Disease in Children: Report of a Case Presenting Cutaneous Pigmentation and Bone Changes, J. Pediat. **1**:754 (Dec.) 1932.

44. Reuben, M. S., and Manning, G. R.: Precocious Puberty, Arch. Pediat. **39**:769 (Dec.) 1922; **40**:27 (Jan.) 1923.

few exceptions, tumors of the pineal gland are of an expanding nature, and they almost invariably produce death. Furthermore, they seldom produce precocious puberty in females. In addition to the negative evidence relating to the size of the adrenal glands in our patient and in the patient of Freedman and Butler, the absence of hirsutism and of excessive masculinity in all the members of the series makes the presence of adrenal tumor highly unlikely. In Freedman and Butler's case the ovaries were inspected and found to be normal. The small cyst which was removed from the ovary did not possess the features of a granulosa cell tumor.

Studies of the excretion of estrogenic and gonadotropic substance have been made in only two cases. The absence of these substances from the urine of the patient of Freedman and Butler (at the ages of 3 years and 6 years) is difficult to interpret. The studies which were made of our patient were not sufficiently extensive to lead to positive conclusions.

Reuben and Manning stated that no case of precocious puberty had been recorded in which the pituitary gland was proved to be primarily at fault. Novak's experience has led him to the same conclusion.[45] Dr. Reuben has recently informed us[46] that continued familiarity with the literature has given him no reason to modify his original assertion. However, the case of the boy reported on by Vickers and Tidswell[47] demonstrates the fact that nonexpanding tumor of the hypothalamic region can produce sexual precocity, at least in males. In this case the pineal and the pituitary gland were normal. Tierney's third patient, also a boy,[48] presented points of clinical similarity to the patient of Vickers and Tidswell. Both patients exhibited mental retardation and attacks of sham rage; neither showed anomalies of pigmentation or osteodystrophy. Without reviewing the evidence in detail, we can state that there is little ground for the belief that any of the patients of our series were suffering from pituitary or hypothalamic tumor.

One of Gaupp's patients had a small adenoma removed from the thyroid gland; another displayed manifestations of transient hyperthyroidism. Our patient exhibits increasing hyperfunction of the thyroid gland. In other cases the state of function of the thyroid gland was not commented on. The interpretation of these data awaits the solution of the problem as a whole.

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45. Novak, E.: Granulosa Cell Ovarian Tumors as a Cause of Precocious Puberty, with a Report of Three Cases, Am. J. Obst. & Gynec. **26**:505 (Oct.) 1933.

46. Reuben, M. S.: Personal communication to the authors.

47. Vickers, W., and Tidswell, F.: A Tumor of the Hypothalamus, M. J. Australia **2**:116 (July 23) 1932.

48. Tierney, J. L.: Pubertas Praecox, M. Clin. North America **6**:31 (July) 1922.

In conclusion, we believe that a variety of miscellaneous etiologic factors may be excluded from complicity in producing the skeletal lesions: osteopsathyrosis, multiple myeloma, generalized sarcomatosis, leukemia, syphilis, tuberculosis and parasitic infestation. Lack of space and the limitations imposed by ignorance prevent a discussion of an ontogenetic theory similar to that suggested by Goldhamer, on which we have meditated fruitlessly, and of the possibility, implied under the discussion of neurofibromatosis, that the syndrome may be the result of a central lesion of unidentified trophic centers. Until further anatomic and physiologic evidence is forthcoming, the problems presented by these patients will probably remain unsolved.

SUMMARY

The case which is described is that of a 9 year old Jewish girl who exhibits true precocious puberty, asymmetrically distributed fibrocystic osteodystrophy of a progressively incapacitating nature and unchanging pathologic pigmentation of the skin. These features have been apparent since the end of the second year of life. In addition, the child has shown evidence of increasing hyperthyroidism since she was 4 years old. The plasma phosphatase activity is increased; in other respects numerous chemical examinations of the blood have given normal results. Balance studies of the calcium and phosphorus metabolism have yielded findings quantitatively similar to those obtained for healthy children; the patient has not shown hypercalciuria. Biopsy of the bone has not provided clearcut information concerning either the precise classification or the etiology of the osseous dystrophy; biopsy of skin has not yielded important data. The evidence derived from measuring the concentration of parathyroid hormone in the blood and of gonadotropic and estrogenic substances in the urine is negative.

Information has been gathered from the literature and from other sources concerning eight, possibly nine, females with an identical condition and five males showing fibrocystic osteodystrophy and pathologic pigmentation of the skin but not precocious puberty. Whether the condition of the males and that of the females are fundamentally related is open to question.

The occurrence of this triad of unusual phenomena in not only one but in several persons suggests strongly the operation of a common causal factor. Critical scrutiny of the available evidence relating to the collected cases does not provide adequate grounds on which to base a satisfactory conjecture concerning the nature of this factor. While the fundamental pathologic condition may be an atypical variety of von Recklinghausen's neurofibromatosis, an unusual type of xanthomatosis or an unidentified disease of the hypothalamic region of the brain, these and other surmises are highly speculative.

News and Comment

UNIVERSITY NEWS

Symposium at Duke University.—Duke University Medical School and Duke Hospital announce a postgraduate symposium on gynecology, obstetrics and pediatrics to be given November 11, 12 and 13. The following speakers are to participate in the symposium: Drs. C. A. Aldrich, Horton Casparis, Willard Richardson Cooke, Julius Hess, Howard Francis Kane, Foster Standish Kellogg, George W. Kosmak, Esther L. Richards and Charles Hendee Smith. Acceptances of several others are pending.

Course for Physicians.—The usual course for physicians is to be given at the University of Vienna throughout the coming year. For information one may apply to Das Kursbüro der Wiener medizinischen Fakultät, Alserstrasse 4, Vienna IX, Austria.

SOCIETY NEWS

Georgia Pediatric Society.—The regular scientific meeting of the Georgia Pediatric Society will be held in Atlanta on Thursday, December 9. Guest speakers will include Dr. Ralph S. Muckenfuss, director, Department of Health, Bureau of Laboratories, New York; Dr. Priscilla White, attending physician, Deaconess Hospital, Boston, and Dr. Joseph Brennemann, professor of pediatrics, University of Chicago, and chief of staff, Children's Memorial Hospital, Chicago.

GENERAL

Death of Dr. Joseph Langer.—On June 24 Dr. Joseph Langer, emeritus professor of children's diseases and director of the first German children's clinic, in Prague, died at the age of 71.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

STANDARDIZATION OF THE IODINE STAIN FOR WET PREPARATIONS OF INTESTINAL PROTOZOA. J. S. D'ANTONI, Am. J. Trop. Med. **17**:79 (Jan.) 1937.

D'Antoni experimented with solutions of iodine and potassium iodide of varying strengths until he determined the strengths that are most satisfactory in staining intestinal protozoa in wet preparations. The preparation of this stain is described in detail. To a 1 per cent standardized solution of potassium iodide is added 1.5 Gm. of powdered crystals of iodine per hundred cubic centimeters. The solution is allowed to stand for four days and is then filtered.

He stresses several points in the preparation of the solution: 1. The solution should be weighed to the fourth decimal place in standardizing the potassium iodide. 2. The concentration of iodine will remain constant only if powdered iodine is used in the solution. 3. To insure saturation, the solution should be allowed to stand for four days before it is used. 4. The solution should always be filtered before being used. 5. The filtered solution should be kept in tight glass-stoppered bottles for periods not exceeding four weeks. However, unfiltered stock solutions can remain for long periods even if stoppered only lightly, and from these solutions filtered ones can be made up on a moment's notice.

The advantages of this new stain are as follows: 1. It will be standard whenever prepared. 2. Once the standardized solution of potassium iodide is made up, the method of preparing the stain is the most rapid of any for iodine stain now in use. 3. The stain shows little or no deterioration over long periods.

BURPEE, Augusta, Ga.

ISOLATION OF PROBABLE PATHOGENIC STAPHYLOCOCCI. G. H. CHAPMAN, C. W. LIEB, C. BERENS and L. CURCIO, J. Bact. **33**:533 (May) 1937.

In searching for pathogenic staphylococci in cultures taken from sources suspected of being pathologic, the authors state, it is customary to plate the cultures on suitable mediums and select colonies for isolation. Tests of pathogenicity are then applied to the pure cultures. Because of the impracticability of testing all colonies, several typical colonies must be selected in the hope that they will include the pathogenic variants. This method has several disadvantages. However, a special medium, consisting of 0.017 per cent bromthymol blue-lactose agar, p_H 8.6, was prepared and found to be of great value for the differentiation of staphylococci. The search for pathogenic types was greatly simplified. On this medium about 98.5 per cent of the pathogenic strains of staphylococci grew luxuriantly, while about 94 per cent of the nonpathogenic ones were inhibited. Inoculations in rabbits were used to check the results, and in this connection it may be stated that, although the pathogenicity of a strain may vary with different species of animals, it is generally conceded that, if the term is used in its broader sense, a strain which is pathogenic for human beings produces dermonecrotic and lethal effects in rabbits.

STOESSER, Minneapolis.

PRODUCTION OF HETEROPHILE ANTIGEN BY CERTAIN BACTERIA AND PLANTS. G. E. ROCKWELL and H. C. VAN KIRK, J. Infect. Dis. **59**:171 (Sept.-Oct.) 1936.

Bacillus mucosus is highly productive of heterophilic antigen, both endogenous and exogenous. Neisseria meningitidis and Haemophilus pertussis contain a moderate amount of heterophilic antigen. Freshly isolated strains of Haemophilus

influenzae contain some heterophilic antigen. Several strains of Brucella abortus, Neisseria gonorrhoeae and Bacillus acnes did not contain any heterophilic antigen.

Some evidence has been produced to show that heterophilic antigen may be capsular as well as somatic in origin.

Spinach, beets and turnips contain some heterophilic antigen. Asparagus, green beans, peas, rhubarb, celery, cabbage, lettuce, carrots, cauliflower and tomatoes do not contain any heterophilic antigen. TOOMEY, Cleveland.

CONCENTRATION AND PURIFICATION OF TOXINS AND TOXOIDS BY ULTRAFILTRATION. F. MODERN and G. RUFF, Rev. Soc. argent. de biol. **12**:70 (May) 1936.

Following the method of James Quingley, the authors describe in detail their methods of purification of diphtheria toxin and toxoids and of tetanus toxin and toxoids. HERRON, Spokane, Wash.

Metabolism; Infant Feeding; Milk and Other Foods

STUDIES OF THE ENERGY OF METABOLISM OF NORMAL INDIVIDUALS: A STANDARD FOR BASAL METABOLISM WITH A NOMOGRAM FOR CLINICAL APPLICATION. WALTER M. BOOTHBY, JOSEPH BERKSON and HALBERT L. DUNN, Am. J. Physiol. **116**:468 (July) 1936.

A study was made of the metabolism of 139 men and 828 women selected as normal persons from a series of more than 80,000 examined at the Mayo Clinic. A nomogram is presented for calculating the basal metabolic rate and determining the probability of normal for the different age and sex groups from 6 to 68 years. NOURSE, Cleveland.

STUDIES OF THE ENERGY OF METABOLISM OF NORMAL INDIVIDUALS: A COMPARISON OF THE ESTIMATION OF BASAL METABOLISM FROM (1) A LINEAR FORMULA AND (2) "SURFACE AREA." JOSEPH BERKSON and WALTER M. BOOTHBY, Am. J. Physiol. **116**:485 (July) 1936.

Berkson and Boothby favor the estimation of basal metabolism from the surface area. NOURSE, Cleveland.

TREATMENT OF INFANTILE SCURVY WITH ASCORBIC ACID. P. LETONDAL, Canad. M. A. J. **35**:646 (Dec.) 1936.

Letondal treated six patients for scurvy with cevitamic acid in the form of tablets, with very good results. All but one were cured within fifteen days. The average dose was one 5 centigram tablet twice a day. Administration of the tablets is advised as a prophylactic measure in children who refuse orange and tomato juice. MOORE, Omaha.

METABOLIC STUDIES OF THE CHANGES IN BODY ELECTROLYTE AND DISTRIBUTION OF BODY WATER INDUCED EXPERIMENTALLY BY DEFICIT OF EXTRACELLULAR ELECTROLYTE. D. C. DARROW and H. YANNET, J. Clin. Investigation **15**:419 (July) 1936.

For creating a deficit of extracellular electrolyte without significant change in total body water, dogs were given an intraperitoneal injection of 100 cc. of 5 per cent dextrose solution per kilogram of body weight. After four hours, when considerable amounts of extracellular electrolytes had diffused into the peritoneal cavity, a volume of fluid approximately equal to that injected was removed with a trocar. Symptoms (especially loss of appetite) and signs of dehydration followed this procedure and persisted until sodium chloride was administered.

Data presented in tables show the shifts of water and electrolytes in the body fluids, determined by direct measurements and by studies of balance. With a large deficit of sodium and chlorine, little restoration of the concentration of serum electrolyte occurred, but with a smaller loss, enough water was excreted almost to restore the concentration of electrolyte in the serum. GUEST, Cincinnati.

ADVANTAGE OF A HIGH PROTEIN DIET IN THE TREATMENT OF SPONTANEOUS HYPOGLYCEMIA. J. W. CONN, J. Clin. Investigation **15**:673 (Nov.) 1936.

Evidence is presented favoring the use of a diet high in protein and low in carbohydrate in the treatment of spontaneous hypoglycemia. It is suggested that the slow rate at which dextrose is liberated into the blood stream during the metabolism of protein is of advantage in the treatment of this condition because (*a*) it avoids hyperglycemia and thus excessive production of insulin and secondary hypoglycemia, (*b*) it makes possible the provision of dextrose over a prolonged period and (*c*) when hypoglycemia is severe, it allows further restriction in carbohydrate than could otherwise be effected. GUEST, Cincinnati.

RÔLE OF SCURVY IN THE ETIOLOGY OF CHRONIC SUBDURAL HEMATOMA. T. H. INGALLS, New England J. Med. **215**:1279 (Dec. 31) 1936.

A closer analysis of five of the cases of so-called idiopathic chronic subdural hemorrhage observed in the Infants' Hospital and the Children's Hospital, Boston, has been attempted. In three of them, x-ray evidence of scorbutic bone changes was found. The epidemiologic and sociologic implications of existing data in this regard have been emphasized.

The following sequence of events seems to be concerned with the production of idiopathic chronic subdural hematoma: An underlying bleeding diathesis on the basis of scurvy is postulated in most cases. Free subdural bleeding is produced by a definite or an insignificant trauma of the head causing disruption of arachnoid invaginations into the dural sinuses or rupture of a bridging vein. Organization and removal of the clot are impeded by the scorbutic process, resulting in a neomembrane surrounding free blood. Repeated trauma and remission and exacerbation of the scurvy modify the disease. GENGENBACH, Denver.

MILK MODIFICATION AND INFANT CONSTITUTION. I. N. KUGELMASS, New England J. Med. **215**:1285 (Dec. 31) 1936.

Comparative studies of so-called standard formulas were made on 337 infants during the first three months of life, with 55 breast-fed infants as controls. The formulas consisted of whole milk, half-diluted milk, evaporated milk (1:1), powdered whole milk (1 tablespoonful to 2 ounces [62 cc.] of water) and powdered lactic acid milk (1 tablespoonful to 2 ounces of water), each reenforced with 10 per cent carbohydrate. Each group maintained on a routine formula was compared with a group of 50 infants given individualized formulas.

The infants consumed more of the processed milk formulas than of the fresh milk formulas, and the maximum was on the side of individualized feedings throughout the period of study. The least number of digestive disturbances was observed with breast feedings and individualized formulas.

Infants of the linear type required about 70 calories per pound of body weight and tolerated concentrated milk mixtures, while infants of the lateral type required about 55 calories per pound of body weight and tolerated diluted milk mixtures better.

Maximum gains in weight were observed in infants on individualized feedings and minimum gains on diluted milk formulas. Infants on breast feedings and on processed milk feedings gained more rapidly than those on fresh milk mixtures.

The gains in height were the same on all types of feeding during the first three months. The incidence of infection was about the same for each group of infants.

Standard routine formulas were effective in over 80 per cent of the infants. The residual nonconformists were infants with latent constitutional disorders—organic, allergic and neuropathic—with either lowered digestive capacities or diminished tolerance. The early recognition of infants of these types led to the displacement of routine by individualized feedings. This group showed the highest percentage of successful infant feeding. Orange juice and cod liver oil were introduced in the third week in each group of between 50 and 60 infants.

GENGENBACH, Denver.

DEMONSTRATION OF A FOLLICLE-STIMULATING HORMONE IN HUMAN COLOSTRUM. V. K. TCHAJKOVJKY, S. A. GUIL and A. K. KOUSNETZOVA, Nourrisson **24**:367 (Nov.) 1936.

Colostrum collected from several parturient women was assayed for its follicle-stimulating hormone and was found to contain from 21 to 83 mouse units per liter. The higher figures were obtained from colostrum collected the first day or two post partum. Other workers have found colostrum rich in the follicle-stimulating hormone and the luteinizing hormone.

These facts seem to point to the important relation between the ingestion of colostrum and the early physiologic development of the sex organs in the newborn infant.

MCCLELLAND, Cleveland.

FEEDING REGIMEN WITHOUT MILK OR POOR IN MILK DURING INFANCY: INDICATIONS FOR IT. B. EPSTEIN and F. WEISS, Paidoterapia **15**:75 (June) 1936.

When artificially fed infants are not able to tolerate milk because of some metabolic or constitutional character, it is necessary to resort to a milk-free feeding or one very poor in milk. The authors offer a pudding (a variation of Moll's biscuit pudding) which has given excellent results in 319 infants.

To make the pudding, mix 333 cc. of water, 80 Gm. of biscuit powder, 1 Gm. of salt, 1 egg yolk, 40 Gm. of sugar, the white of 1 egg, well beaten, and 20 Gm. of butter. Cook for forty-five minutes in a double boiler.

The indications of its use are: spasmophilia, rebellious eczema during the second six months of life, constitutional anorexia, nutritional anemia, disturbances produced by overfeeding of fats, digestive upsets due to cow's milk, enteric infections and nutritional parenteral infections.

HERRON, Spokane, Wash.

ACETONEMIA AND ACETONURIA IN INFANCY. A. M. V. DE GANDOLFO HERRERA and H. M. BERISSO, Rev. méd. latino-am. **22**:299 (Dec.) 1936.

The authors studied the variations in the quantities of ketone bodies in such pathologic states as pneumonia, bronchopneumonia, septicemia, meningitis, osteomyelitis and other suppurative processes, as well as in prolonged states of debility, such as are observed with certain forms of tuberculosis and with digestive disorders. The principal object of this study was to develop a simple technic with a minimum of error; the method of Shaffer was used for urine, and an adaptation of de Engfeldt's method, for the blood. These procedures are described in detail.

DWYER, Kansas City, Mo.

OBESITY IN CHILDHOOD. L. FREY, Arch. f. Kinderh. **109**:1, 1936.

Two cases in children are described. The obesity was reduced satisfactorily on lessened caloric intake, without endocrine therapy.

CRANE, Washington, D. C.

Applied Colloid Science in Infant Nutrition. Ullmann, Arch. f. Kinderh. **109**:84, 1936.

Consideration of the physical-chemical characteristics of human milk and cow's milk leads to the conclusion that the digestibility of the latter as used in infant feeding can be improved by raising the p_H above 7 or by adding highly dispersed protective colloids to buffer the casein, thus insuring a more gradual and softer precipitation of the casein.

Crane, Washington, D. C.

Agar-Milk Treatment of Dyspepsia of Scheer. H. Rübenhagen, Arch. f. Kinderh. **109**:193, 1936.

Scheer fed 145 infants with dyspepsia, an agar-milk mixture. The results were uniformly good. The number of stools decreased promptly, and gain in weight began even before the dyspepsia was completely cured.

Crane, Washington, D. C.

Sport and Nutrition. C. von Noorden, Med. Klin. **32**:993 (July 24); 1036 (July 31) 1936.

Von Noorden gives an elementary discussion of diet in the training of athletes and presents neither new facts nor new ideas.

Dooley, New York.

Old and New Problems in Dietetics. W. Falta, Wien. klin. Wchnschr. **49**: 1449 (Nov. 27) 1936.

Falta, reviewing the subject, lists the basic facts about the balanced diet. The amount of food required depends on the amount of muscular work done. Bedridden people need only about 1,800 calories daily; men doing physical labor may require 4,000 or more. Determining the patient's requirements is the greatest difficulty. Normally, appetite is the guide. The author believes it should be considered in illness also. Even diabetic persons (unless inactive and inclined to be overweight) in his opinion should be allowed fats according to their appetite.

In cases of true obesity (as distinguished from overweight caused by glandular disturbances), the author has found that the so-called Hollywood diet brings about remarkable reductions in weight; also, except for occasional bradycardia, it is practically harmless to health. When obesity is not a question of fat but of water-logged tissues, a salt-free diet will cause a quick cure.

All vitamins are subject to destruction by heat and oxidation. Dried fruits have practically no vitamin content. Preserved fruits and pasteurized milk contain less of vitamins than milk in the raw state. Vitamin B_1 is lost when grains are milled, although a good percentage remains in the bran. The whiter the flour the lower is the value in vitamins. The storing of potatoes causes loss of vitamins.

The question of salt in the diet must be answered after considering its effect on the blood and nervous system. In the first place, there are various kinds of salt. An excess of sodium salts in the blood causes absorption of water; an excess of potassium salts, expulsion of water. In relation to the nervous system, sodium acts as a mild sedative, potassium as a stimulant.

In spite of the fact that dietetics, more than any other field of medicine, has suffered from exaggerated ideas, fads and fanaticism, it is a science based on solid ground, and it has shown and will continue to show many roads leading to the prevention and cure of disease.

Abt, Chicago.

Determinations of the Water Content of the Blood in 1,239 Boys and Girls, Pupils in Secondary Schools. T. Ryô, Keijo J. Med. **7**:426 (Oct. 31) 1936.

The boys and girls studied in this large group were between 12 and 19 years of age. The content of water in the blood averaged 79.5 per cent for the 12 year

group. There was a slight rise as a rule in the thirteenth, fourteenth and fifteenth years, although this never reached as high as 80 per cent. Following the fifteenth year the water content showed a gradual decrease, approaching 78 per cent at the age of 19 years. The possible relationship of the increase in water content shown in the thirteenth, fourteenth and fifteenth years to the onset of puberty is discussed.

LESLIE, Evanston, Ill.

Vitamins; Avitaminoses

RÔLE OF THE THYROID IN THE CALORIGENIC ACTION OF VITAMIN D. H. DEUTSCH, C. I. REED and H. C. STRUCK, Am. J. Physiol. **117**:1 (Sept.) 1936.

The authors point out that vitamin D probably has many effects in addition to its action on the calcium-phosphorus metabolism, such as restoration of normal oxygen consumption in rickets. In experiments on two dogs submitted to thyroparathyroidectomy the basal metabolism was not markedly augmented with large doses of vitamin D, as in normal dogs. Whether this thyrotropic effect is due to direct action of vitamin D on the thyroid or to indirect action through the anterior lobe of the pituitary is being further investigated.

NOURSE, Cleveland.

FURTHER STUDY OF THE RELATION OF THE ADRENAL CORTEX TO VITAMIN C. J. E. LOCKWOOD, D. R. SWAN and F. A. HARTMAN, Am. J. Physiol. **117**:553 (Nov.) 1936.

An extract of adrenal cortex relatively free from vitamin C was found to ameliorate the symptoms of avitaminosis C. The authors therefore conclude that cortical hormone or some unknown substance from the adrenal cortex delays the onset of scurvy.

NOURSE, Cleveland.

BACTERIAL RESISTANCE IN B-DEFICIENT DOGS. S. B. ROSE and W. B. ROSE, J. Infect. Dis. **59**:174 (Sept.-Oct.) 1936.

According to these authors, animals that had been rendered partially deficient in vitamin B appeared to be more susceptible to artificial infection with Staphylococcus aureus than animals fed an adequate amount of this vitamin.

TOOMEY, Cleveland.

A QUANTITATIVE STUDY OF THE UTILIZATION AND RETENTION OF VITAMIN B BY YOUNG CHILDREN. ELIZABETH M. KNOTT, J. Nutrition **12**:597 (Dec.) 1936.

Eight normal young children comprised the group which was studied for utilization of vitamin B as affected by various levels of ingestion during twenty-three periods of metabolic study. Utilization of vitamin B was studied through biologic assay with rats of the amounts of vitamin B in the food and excretions of children receiving weighed diets.

The results indicate that the intakes which produced the highest retentions were from six to seven times greater than the minimum requirement for preventing beriberi. Increasingly higher retentions were obtained with higher intakes for each level of ingestion studied.

The author concludes on the basis of the ingestions giving highest retentions that the optimum requirement of vitamin B by young children is about 40 Sherman-Chase units per kilogram of body weight per day. MUNNS, Winnetka, Ill.

THE PROPHYLACTIC VALUE OF VITAMIN D IRRADIATED AND VITAMIN D YEAST-FED MILK. R. CANNON ELEY, E. C. VOGT and MARY G. HENDERSON, New England J. Med. **215**:110 (July 16) 1936.

This study was undertaken in an effort to determine the relative prophylactic value of two types of vitamin D milk when it is employed as the only source of

antirachitic substances in artificially fed infants; i. e., it was a "preventive" and not a "curative" study.

Twenty-six infants were studied. All were placed on a diet based on vitamin D milk within the same week, and therefore it was possible to follow the entire group for five months. The age of the patients at the beginning of the study varied from 2 to 12 weeks. The group contained one set of twins and three premature infants. The infants were subjected to a physical examination once each month. Measurements of the fontanel, head and chest, circumference, length and weight were noted. Notes were also made in regard to dentition, muscular development and activity of the baby. Roentgenograms of both forearms were taken by a uniform technic at the Children's Hospital of Boston once each month and compared with the results of the physical examination. Chemical determinations of serum phosphorus and calcium were not made, as one of the purposes of this study was to utilize only those procedures which are readily available to any practicing physician.

The milk, which was delivered free to each family every morning, contained 135 and 432 U. S. P. vitamin D units, the former being obtained by irradiation and the latter by feeding the cattle known quantities of yeast. Thirteen infants received the irradiated milk and fourteen the milk from yeast-fed cows. Each mother kept a diary in which she recorded the exact amount of the formula ingested by the infant at each feeding, thereby making it possible to determine the number of vitamin D units taken each day through the period of study. The formulas consisted of whole milk, corn syrup and water. Antiscorbutic substances in the form of orange or tomato juice were added to the diet at appropriate periods, as were cooked cereals and strained vegetables. Thus, the diet met all the known nutritional, mineral and vitamin requirements, with the exception of vitamin D, which was supplied solely from the milk.

The results of this study showed that none of the infants acquired rickets detectable either by clinical or by roentgen examination, regardless of which type of milk they received. In the majority of instances the rate of growth was within the accepted curve of normal growth and development.

GENGENBACH, Denver.

SOME CONSIDERATIONS ABOUT VITAMINS B AND G AND PELLAGRA AND OTHER MANIFESTATIONS DUE TO A LACK OF THESE VITAMINS. A. RAMOS ESPINOSA, Rev. mex. de puericultura **5**:935 (Dec.) 1935.

The common Mexican foods for children and adults consist nearly exclusively of carbohydrates and are very poor in vitamins, especially vitamins B and G. These two circumstances, in association, produce pathologic disturbances in the body, which, however, in most of the cases do not give rise to manifest symptoms and have been little studied. It is up to the doctors to get away from ancestral feeding customs and give adequate diets and dietary instructions.

HERRON, Spokane, Wash.

THE PHOTO-ACTIVITY OF FOODS IRRADIATED BY THE SUN. A. H. ROFFO and A. E. ROFFO JR., Rev. Soc. argent. de biol. **11**:118 (May) 1935.

The Roffos subjected different animal foods, as bacon, pork sausage, blood, bone marrow, cheese, lard, egg yolk, butter, cod liver oil and milk, to solar radiation and found that this produced strong photo-activity, while in meat it did not produce any. Irradiation of the same group by ultraviolet rays produced no photoactivity.

In such products as bananas, oranges, potatoes and other vegetables, the sun's rays produced no photo-activity. In this group, also, ultraviolet rays produced no photo-activity. The actinic rays responsible for the activation lie between 2,260 and 3,350 Angström units.

HERRON, Spokane, Wash.

HISTOLOGIC STUDIES OF THE EFFECTS PRODUCED BY LARGE DOSES OF CAROTENE, CARROTS AND VITAMIN A. TOMAS OCAÑA, Rev. Soc. argent. de biol. **11**:147 (May) 1935.

Large doses of carotene did not produce renal lesions, and the modified lesions of the liver encountered were thought to be due to the excessive fat. The animals treated with lipoids, carrots and the nonsaponifiable fraction of the same presented perilobular and central hepatic lipoidosis. The cutaneous lesions observed in the animals treated with vitamin A were marked acanthosis, with a tendency to papillomatosis, and keratosis, parakeratosis and atrophy of the hair follicles.

HERRON, Spokane, Wash.

CONTRIBUTION TO THE CUTANEOUS MANIFESTATIONS OF VITAMIN A DEFICIENCY. F. REISS, Chinese M. J. **50**:945 (July) 1936.

Cutaneous lesions due to vitamin A deficiency have only occasionally been reported from China, but this report from the department of dermatology of the National Medical College of Shanghai, China, concerns the disease in seven boys and girls aged 15 to 19 who were employed in a rug factory. Some of them complained of night blindness, though usually it was only temporary and had no relation to the severity of the cutaneous lesions. The cutaneous manifestations were dryness and in some cases a papular eruption. The papules were from 0.1 to 0.5 cm. in diameter; they were hemispherical and firm, seldom containing pus. The papules were hyperpigmented, with horny processes containing curled and broken hairs. The most common site was the posterior aspect of the neck. Sometimes there existed involvement of the nails and also of the mucous membrane, the latter presenting lesions of the lips resembling perlèche. Xerosis of the skin is not a prodromal sign, but it is a feature of hypovitaminosis A.

NEFF, Kansas City, Mo.

PROGNOSIS OF SPASMOPHILIA. P. J. NORDENFELT, Acta pædiat. **19**:187, 1936.

The remote prognosis for infantile tetany remains uncertain. The earliest authoritative studies are those of Thiemich and Birk and of Potpeschnigg, which were published in 1907 and 1908, respectively. Both investigations led to the conclusion that only a small proportion of infants treated for spasmophilia in infancy develop into mentally normal, emotionally stable adults. This dour outlook has been confirmed by other observers. On the other hand, dissenting opinions of a more optimistic character are found in some of the contemporary textbooks of pediatrics. The newer point of view is supported by Hjärne's observations on a small number of cases, which were published in the *Acta pædiatrica* in 1931.

During the twelve year period between 1917 and 1928, 169 infants were treated for tetany in the Sachsska Barnsjukhuset, Stockholm. In the majority of cases the clinical diagnosis was confirmed by measurements of the electrical excitability of peripheral nerves; during the last two years of the period covered by the study the serum calcium determined in "a number of cases." In 143 cases the diagnosis appeared incontrovertible in retrospect; in 21 cases the correctness of the diagnosis was open to question, although the author accepts the cases after discussion. One hundred and forty-three patients were presumed to be alive at the time of the study; of these, 81 (57 per cent) were examined. Of the patients who were no longer alive, in only 3 (1.8 per cent) could death be ascribed to spasmophilia.

Of the 81 children who were examined, only 5 had had convulsions after leaving the hospital: the study revealed no positive correlation between infantile tetany and juvenile epilepsy.

Nordenfelt paid particular attention to the mental development and to the presence of stigmas of a neuropathic constitution. Of the 81 patients, 42 per cent were found to be mentally and emotionally sound. About 9 per cent exhibited a severe mental defect, and about 9 per cent were moderately retarded. Forty per

cent of the children showed evidence of emotional instability, although in most cases this was moderate.

Critical scrutiny of these data leads to the conclusion that infantile tetany is not an immediate cause of a juvenile mental defect; however, the possibility cannot be denied that cerebrally inferior infants possess an increased disposition to spasmophilia. The incidence of emotional instability without mental retardation was found to be no higher in the group of patients examined than in persons of the same social class who had not previously had tetany. McCUNE, New York.

CEVITAMIC ACID CONTENT OF SOME COMMON FOODSTUFFS. K. UTHEIM TOVERUD, Norsk mag. f. lægevidensk. **97**:1288 (Dec.) 1936.

Toverud has analyzed milk, meat and vegetables for the cevitamic acid content by the method of Bird, Harris and Ray. The results tabulated correspond to those of earlier investigators. There was a small amount of oxidized, biologically active cevitamic acid present in most of the foodstuffs analyzed. Cooking does not always reduce the amount of cevitamic acid; some vegetables (potatoes and carrots) may even show an increase after from ten to fifteen minutes' cooking owing to the fact that cevitamic acid is in part present in a combined form which is split by cooking. WALLGREN, Göteborg, Sweden.

Hygiene; Growth and Nutrition; Public Health

PHYSICAL WELFARE OF YOUTH. LEONARD P. LOCKHART, Brit. M. J. **2**:1254 (Dec. 19) 1936.

Lockhart writes an inspirational paper, outlining what he calls "creative living." The obvious objective of his work is to make as nearly perfect adults of young persons as possible. The subject is discussed under several headings, the first being "The Need of Incentives." He feels that incentive is essential to hearty cooperation on the part of youths with any program of better physical development. He next outlines the "Essentials of Good Nutrition" and admits that any standard of nutrition is more or less fallible. Certain criteria, however, are sufficient to guide one in appraisal. He finds out the difficulty of securing adequate food in certain social-economic strata of society. Likewise the lack of good preparation of food frequently plays an important part and raises the value of canned food, certainly from the standpoint of time saving. The question of sleep comes in for a liberal share of responsibility in nutrition. The next heading, "Preliminary Steps," outlines certain necessary introductory features. An ordered sequence of food and living is outlined and stressed. The aims of physical education must be understood. They differ with different parts of the country and with different peoples and races. Finally, emphasis is placed on newer ideals. The questions of backwardness and delinquency as related to the whole subject are emphasized.

ROYSTER, University, Va.

FERTILITY AND ITS RELATIONS TO SOCIAL CONDITIONS. K. MITRA, J. Hyg. **37**: 108 (Jan.) 1937.

A rapid decline in birth rate has been reported in nearly all countries of western Europe. In London between 1901 and 1931 it fell from 29.1 per thousand living persons to 15, a more rapid fall than that during the preceding thirty years.

Studies by Heron thirty years ago indicate that the drop in birth rate was greatest in the higher social strata and least in the less desirable ones. In a careful statistical study Mitra confirms Heron's conclusions in general. However, there is less divergence between the two groups than formerly in infant mortality rates; i. e., infant mortality is perhaps ceasing to be so sensitive a measure of unfavorable social conditions but is still sensibly associated with the degree of overcrowding. JANNEY, Wauwatosa, Wis.

NEGLECTED MOTHERS. O. RODRÍGUEZ, Bol. Inst. internac. am. de protec. a la infancia **10**:365 (Jan.) 1937.

Rodríguez discusses the problem of proletarian mothers from the point of view of the funds available to solve situations which are difficult, but he points out that the condition of unmarried, widowed or divorced expectant mothers, whom he calls neglected mothers, is still worse. The importance of the first of these three groups can be measured by the fact that some time ago 70,000 illegitimate children were born in the country every year. The principal factors in such a state of things are ignorance, poverty and surrounding immorality.

To counteract the sad consequences of the neglect of such mothers and their children, Buenos Aires has the Institute of Maternity of the Sociedad de Beneficencia, with its shelters for pregnant women and recent mothers; there are like divisions at the Eliseo Cantón Maternity, at the Patronato de la Infancia and at the Assistencia Publica. The peculiarity of the shelters for pregnant women is that they allow the future mothers to work and earn some money which will lessen the difficulties which they may meet on leaving the maternity homes with their children.

All these measures for neglected unmarried mothers do not attack the causes of the evil: It is necessary to adopt laws that make investigation of paternity compulsory and to establish the father's obligation to maintain his illegitimate child and its mother from the conception of the child to its becoming of working age.

Furthermore, it will be necessary, in order to do efficient work, to coordinate the efforts of all institutions, either public or private, which protect mothers.

FROM THE AUTHOR'S SUMMARY.

THE SUPERVISION OF SCHOOL HYGIENE AND SANITARY EDUCATION. F. FIGUEIRA DE MELLO, Bol. Inst. internac. am. de protec. a la infancia **10**:378 (Jan.) 1937.

If the state makes school attendance compulsory, it must on its side care for the health of the children, preventing in particular contagious diseases. The condition of the child of school age is a delicate one on account of growth and development and requires the solicitous care of the doctor, who alone is able to make an interpretation of facts that will permit correction of errors, suppression of deficiencies and cure of defects in due time.

In the present state of school progress, the work of the teacher cannot be conceived apart from that of the doctor, since both officers must cooperate in order to obtain compliance with the principles of health education.

FROM THE AUTHOR'S SUMMARY.

THIRD INTERNATIONAL CONGRESS OF OPEN AIR SCHOOLS. A. MOLA, Bol. Inst. internac. am. de protec. a la infancia **10**:404 (Jan.) 1937.

Commenting on the importance of the Third International Congress of Open Air Schools, which was attended by delegates from twenty-five countries, Mola points out the stress that Germany lays on physical education in endeavoring to give children a harmonious intellectual and physical education.

From the teachings of the congress, as established by the conclusions which were published in a former number of this bulletin, Mola presents the following points:

1. Open air schools should be under the control of a doctor, since their dependence on medical knowledge and supervision should be more complete. Considered as agencies of social medicine, such schools give the impression that they are sui generis clinics.

2. Since these schools are centers of school hygiene, it is absolutely necessary that they should be provided with the services of social visitors.

3. Another important point is the need for establishing dental clinics in these schools.

4. They should also be provided with autobuses to insure regular attendance of children and to prevent their becoming tired, particularly the smaller ones, from having to walk long distances.

FROM THE AUTHOR'S SUMMARY.

Prematurity and Congenital Deformities

THE CARE AND FEEDING OF THE PREMATURE INFANT, WITH SPECIAL REFERENCE TO SIMPLE MILK MIXTURES. A. TOW, M. Clin. North America **20**:951 (Nov.) 1936.

In Tow's opinion breast milk is not so essential to the proper nourishment of premature infants as is generally taught. Granting that it is the most desirable food for the new-born infant, nevertheless it is possible successfully to feed premature infants on simple cow's milk mixtures. During the first week of life the objective should be to maintain life, not to produce a gain in weight. Fluids should not be forced, but given in small amounts at frequent intervals. The amounts given should be gaged by the infant's capacity and desires rather than by theoretical considerations of fluids needs. The appetite of the premature infant is capricious and should be respected. If the infant will not take the nipple, fluids should be given by a medicine dropper with a soft rubber extension. Gavage should not be used as a routine, and hypodermoclysis is only exceptionally necessary. If breast milk is available, it is reenforced with from 7 to 10 per cent carbohydrate. Simple mixtures of cow's milk and calcium caseinate, with concentrations of carbohydrate of from 10 to 17 per cent, were found satisfactory. Until sufficient fluid is taken at regular feedings, 5 per cent sugar solution is given midway between feedings.

EUGENE SMITH, Ogden, Utah.

CONGENITAL DEFECT OF THE PECTORAL MUSCLES. R. R. LITTLE, New England J. Med. **214**:934 (May 7) 1936.

There appears to be no predominance of the occurrence of pectoral defects on the right or on the left side. Only one case has been reported in which the condition was bilateral.

The affected side of the thorax is flattened, and the ribs are plainly visible and palpable beneath the skin and subcutaneous tissue. It is said that deformities in the nipple and breast are often present, and complete absence of the breast and nipple has been reported. There may be defects in the underlying ribs, the cartilaginous portions often being distorted or absent.

The author's case was observed in a boy aged 6 years, who was admitted to a sanatorium for a childhood type of tuberculosis. Photographs are shown.

GENGENBACH, Denver.

CONGENITAL PATENT URACHUS. P. J. MAHONEY and D. ENNIS, New England J. Med. **215**:193 (July 30) 1936.

At the Children's Hospital and the Infants' Hospital, Boston, with a total of 200,000 admissions, the diagnosis of congenital patent urachus (with discharge of urine at the umbilicus) has been made 3 times. There have been 2 cases of a persistent urachus which did not communicate with the bladder. In a series of 3,466 necropsies from 1914 to 1935, persistent urachus has been reported as an incidental finding 6 times. In none of these cases was there an umbilicovesical fistula.

In the first of the 3 cases diagnosed, the patient was operated on with success; in the second, the patient died shortly after operation from peritonitis subsequent to an infection already present in the urachus on admission; in the third case, the patient recovered after operation. This case is presented in detail, with a cystogram.

GENGENBACH, Denver.

ANOXEMIA IN PREMATURE INFANTS. W. P. BUFFUM, New England J. Med. **215**:390 (Aug. 27) 1936.

The purpose in this paper is to show that there is evidence that many, if not all, of the small premature babies that do not do well during the first month of life are anoxemic and benefit by an increased oxygen content in the inspired air

Premature infants in poor condition are put in Burgess oxygen boxes as soon as they arrive from the delivery room; they are kept there until their condition is satisfactory, and they are put back again if they become cyanotic.

If the patient is suffering from anoxemia, continuous administration of oxygen is indicated. Premature babies that do not gain in weight during the first month of life are helped by oxygen.

GENGENBACH, Denver.

THE MARRIAGE HEALTH LAW AND THE CONGENITAL BODY DEFORMITIES. M. LANGE, München. med. Wchnschr. **83**:1420 (Aug. 28) 1936.

Apparently it is necessary to obtain a health certificate to marry in Germany. The certificate can be refused if a person has a bodily deformity which might be transmitted to an offspring. Lange discusses at length the advisability of such a law and also points out that many deformities are not hereditary. He raises the question whether an outwardly healthy person coming from a family with some hereditary deformity should be permitted to marry.

BRAHDY, Mt. Vernon, N. Y.

MICROCEPHALIC FETUS WITHOUT EYES AND NOSE AND WITH SERIOUS DEFECTS OF THE FOREBRAIN, CEREBELLUM, INNER EAR AND ENDOCRINE GLANDS. G. ILBERG, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:1 (Oct.) 1935.

Ilberg reports the case of a 6 month fetus that died immediately after birth. The skull was small (13 cm. long and 4.5 cm. wide). There were no fontanels or sella turcica. The jaw was prognathous and the anus imperforate. The right external ear was poorly developed, there being merely four soft prominences at the site at which the ear should have been. The external auditory canals were not patent. The eyes and nose were absent. Clubfoot was present bilaterally. In the midfrontal region there was a vertical indentation, 2.5 mm. long, from the end of which a somewhat deeper groove extended in a forklike manner 2.5 cm. to the right and to the left, respectively. The cerebrum and cerebellum were absent. No hypophysis was seen. The falx cerebri, tentorium cerebelli, olfactory bulbs and optic and oculomotor nerves were absent. The thyroid, uterus, ovaries, adrenal glands and pancreas were very small. The cochlea was absent bilaterally. Some development of the semicircular canals was seen on the right side. The large olives were both absent. Of all cerebellar structures only the corpus dentatum was observed. The facial nuclei were poorly developed. There was no microscopic evidence of syphilis. Reports of only two similar anomalous fetuses were found in the literature (Raddatz, 1829, and Ahlfed, 1882). Ilberg notes the following facts in the family history of the woman who gave birth to this abnormal fetus: Two siblings had epilepsy in early life; her father and mother were deaf-mutes; the father was alcoholic, sadistic and unquestionably psychopathic, and both grandparents were alcoholic. These factors may play a rôle in accounting for this unusual developmental anomaly.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

TREATMENT OF PREMATURE INFANTS WITH HORMONES, COLOSTRUM AND BLOOD SERUM OF GRAVIDAS. E. DAPSY, Orvosi hetil. **80**:1136 (Nov. 28) 1936.

In the gynecological clinic in Debreczon, Hungary, premature infants were treated with hormones (extract of the anterior lobe of the pituitary body and extract of corpus luteum), expressed colostrum or blood serum from pregnant women. The blood serum was given to those whose mothers did not have sufficient milk. It was given in the form of food mixed with mother's milk (20 cc. a day). To infants whose mothers had sufficient milk the serum was given by intramuscular injection (5 cc. a day). Dapsy seems to be content with the results of all these three methods, and now all three are used together.

GÖTTCHE, Budapest, Hungary.

THE DEVELOPMENT OF PREMATURE INFANTS. G. VON SYDOW, Upsala läkaref. förh. **42**:21, 1936.

At the pediatric clinic of Upsala 124 premature infants who were cared for during their new-born period were examined from three to nine years later; 16 had died, and 10 could not be found. Of the remaining 98 children, 7 (all of them born with a weight of less than 2,000 Gm.) showed severe neuropsychiatric symptoms, e. g., epilepsy, Little's disease, idiocy, imbecility or deaf-mutism. It is concluded that, in comparison with children in the general population, there is a certain degree of physical underdevelopment statistically probable in premature infants when they have reached school age, but in other respects there is no cause to regard them as physically or mentally inferior at that age.

WALLGREN, Göteborg, Sweden.

DYSOSTOSIS CLEIDOCRANIALIS HEREDITARIA. J. C. J. BURKENS, E. H. LA CHAPELLE and J. GROEN, Nederl. tijdschr. v. geneesk. **80**:5547 (Dec. 12) 1936.

This is a description of a family with hereditary cleidocranial dysostosis, showing greatly varying clinical symptoms. The authors also studied another family with the same condition. The dysostosis was described by La Chapelle in 1918. As regards etiology, several theories are discussed. In cleidocranial dysostosis there is a modified structure of the bone, and there is absence or retardation of the formation of normal bone and muscles at the places of predilection. The cause of the disease should be a gene. The theories of Marie-Sainton and of Murk Jansen cannot be maintained. The deviation arises as a mutation and after that is dominantly hereditary.

VAN CREVELD, Amsterdam, Netherlands.

New-Born

A STUDY OF B. COLI MUTABILE FROM AN OUTBREAK OF DIARRHEA IN THE NEW-BORN. A. D. DULANEY and I. D. MICHELSON, Am. J. Pub. Health **25**:1241 (Nov.) 1935.

An outbreak of severe diarrhea with a mortality of 47 per cent occurred in the nursery of the Memphis General Hospital during the winter of 1933-1934. Symptoms began on the fifth to ninth days of life, with fever, diarrhea, loss of weight and vomiting. The stools were watery and yellow, and contained no blood, pus or mucus. Bacillus coli-mutabile was isolated from the stools of 67 per cent of the sick infants. This organism also was found, together with other organisms, at postmortem examination. It fermented lactose only after it had been grown on Endo agar plates for thirty-one hours; after ninety-six hours 90 per cent of the colonies were red. Evidence is presented to show that all strains of the organism isolated from sick babies form a homologous serologic group. It is possible that B. coli-mutabile was a secondary invader and not the primary cause of the outbreak.

MCBRYDE, Durham, N. C.

TETANY OF THE NEW-BORN. M. D. JACOBY, J. Michigan M. Soc. **35**:496 (Aug.) 1936.

Jacoby raises the question whether tetany occurs during the neonatal stage of the infant's life. After considering diagnosis and treatment, he gives the histories of three infants presenting a syndrome which he entitles "typical tetany in childhood and adult life."

CAREY, Detroit.

FRACTURES IN THE NEW-BORN. A. THORNDIKE JR. and F. R. PIERCE, New England J. Med. **215**:1013 (Nov. 26) 1936.

The old teaching that mere fixation is the only treatment required to produce good results in fractures of this class is no longer considered satisfactory.

It was a revelation to find children with birth fractures coming to the hospital at from 12 to 18 months of age because of unilateral bowleg.

The proportion of birth fractures to all fractures as seen in a review of 6,000 cases at the Children's Hospital, Boston, was 113:6,000, or approximately 1:60. Birth fractures are, in the large majority of cases, accidents occurring in difficult obstetric manipulations. In this series they occurred, in most cases, in large babies. Not one instance of true intra-uterine fracture was found. The disease entities of osteogenesis imperfecta, fragilitas ossium and the dysostoses should not be considered as included in true birth fractures.

The pleas for more adequate treatment of fractures of the new-born have in view (1) early diagnosis, (2) early manipulative alinement of the fragments involved and (3) proper fixation. An outline of methods of fixation, with illustrations, is presented.

GENGENBACH, Denver.

JAUNDICE AND ANEMIA WITH RECOVERY IN SUCCESSIVE NEWBORN SIBLINGS. R. F. NETTER, New York State J. Med. **36**:1843 (Dec. 1) 1936.

The mother of the patients had previously given birth to two normal children. The third child became jaundiced and died on the third day. Another child survived but ten hours. Three subsequent children were under close observation, and complete histories are presented. They all had jaundice, anemia and enlargement of the liver and spleen. A diagnosis of erythroblastic anemia of the new-born was made. The children recovered after repeated transfusions.

AIKMAN, Rochester, N. Y.

SCLEREMA NEONATORUM, LOCALIZED TYPE. MARIE KRESTIN, Proc. Roy. Soc. Med. **30**:412 (Oct.) 1936.

A case was reported in a boy of 7 weeks. There was a large indurated swelling over the head of the right and of the left great trochanter. Both shoulders showed similar patches of thickening over the deltoid muscles. The patches of thickening were in the subcutaneous tissue, were irregular in shape, were of symmetrical distribution in the body and were over bony prominences of joints. The overlying skin was not discolored, inflamed or tender.

WILLIAMSON, New Orleans.

SYPHILITIC LESIONS OF THE CORNEA AND THE CONJUNCTIVA IN A NEW-BORN INFANT. NICOLAS, P. BONNET, GONNET, BANSILLON and COLRAT, Bull. Soc. d'opht. de Paris, February 1936, p. 97.

In the corneal ulcers of a premature infant the spirochete was observed. The Wassermann reaction of the blood had been negative. In the first few days the infant showed conjunctivitis of each eye, that in the left eye being more marked, with edema of the lids, chemosis and staphylococcic suppuration. Ulcers of the corneas were present, and, in addition, interstitial infiltration with vascularization. Consultation with Professor Nicolas, of the department of diseases of the skin, resulted in a diagnosis of syphilis, and the treponema was observed in corneal scrapings. The question of hereditary syphilis is discussed. The liver and the spleen were not enlarged, and there were no buccal lesions. No chancre was found in the examination of the passages. An isolated enlarged gland was found in the maxillary angle. This was very hard. General treatment, consisting of mercury rubs, was given. Recovery was immediate. The mode of contamination remains obscure. The Wassermann reaction of both parents was negative.

MAYER, Chicago. [ARCH. OPHTH.]

PNEUMOTHORAX IN THE NEW-BORN. M. PÉHU, Paris méd. **2**:335 (Nov. 7) 1936.

With the use of roentgen rays it has become evident that pneumothorax occurs in the new-born more frequently than was hitherto thought. It may be complete or partial and should be considered in any case of dyspnea and cyanosis. Rupture of the alveoli may be caused by obstetric injury, by efforts at resuscitation or by septic infarcts.

LESLIE, Evanston, Ill.

TASTE AND SMELL IN THE NEW-BORN. F. STIRNIMANN, Rev. franç. de pédiat. **12**:453, 1936.

On the basis of the vasomotor and motor reflexes, Stirnimann finds that the new-born infant is capable not only of perceiving gustatory stimuli but of distinguishing them. The infant is also capable of responding to olfactory stimuli but not as consistently as to gustatory ones. Nasal taste is more developed than smell itself. The latter serves to complete taste. The examinations have shown not only simple reflex responses but also more complicated reactions which one must range among psychic manifestations.

LESLIE, Evanston, Ill.

HEMOGLOBIN METABOLISM IN THE NORMAL NEW-BORN. G. ROSSI and ANNA DORDI, Lattante **7**:566 (Nov.) 1936.

From 23.04 to 55.7 mg. of bilirubin was found in the meconium passed by infants during the first three days of life. The bilirubin tended to diminish in amount as the meconium was replaced by the normal infant stool. Urobilin (bilin) was found in the meconium of 4 of 7 infants (0.9 to 6.24 mg.) and was usually absent from the stools of breast-fed infants. The urobilin in the meconium is probably of maternal origin, as urobilin is formed from bilirubin by bacterial action.

The hemolytic index in the first two weeks of life was approximately 1.0.

HIGGINS, Boston.

BIOMETRIC DATA AND THE MORPHOLOGIC MEDIAN OF THE CANTANESE NEW-BORN. G. ERNANDEZ, Lattante **7**:600 (Dec.) 1936.

Anthropologic data were gathered on 120 normal new-born children from Catania and the neighboring province; 60 of these were boys, and 60 were girls. Comparisons are made of these data on Catanese children with data previously published from Palermo, Naples, Rome, Florence, Bologna, Padua, Pavia and Sassari. The new-born infants from the province were somewhat better developed than those from Catania itself.

HIGGINS, Boston.

SPONTANEOUS PNEUMOPERITONEUM IN A NEW-BORN INFANT. H. TUNGER, Monatschr. f. Kinderh. **67**:264 (Nov.) 1936.

On the fifth day after birth an infant presented a very rigid abdomen. X-ray pictures, of which three are shown, revealed pneumoperitoneum. A spontaneous cure occurred in eighteen days. The etiology is unknown.

GERSTLEY, Chicago.

ACUTE DERMATITIS IN THE NEW-BORN. E. FLUSSER, Monatschr. f. Kinderh. **67**:279 (Nov.) 1936.

Flusser gives a brief discussion of the types of dermatitis occurring in the new-born. He finds two types: pyoderma and dermatitis exfoliativa. The treatment in all cases is feeding on breast milk, protection against decubitis, opening of abscesses and prevention of overheating. He also recommends saturating the wound with powdered sugar. He says this treatment was successful in the war, but for some reason has fallen into disuse.

GERSTLEY, Chicago.

ETIOLOGY OF RUPTURE OF THE LIVER IN THE NEW-BORN. F. J. SCHMITT, Ztschr. f. Geburtsh. u. Gynäk. **114**:70 (Dec.) 1936.

Schmitt reviews the literature on the subject and discusses three cases of his own. He concludes that rupture of the liver is very rare, that it is usually produced by mechanical factors causing trauma during birth but that occasionally it

is found following normal labor in which there has been no reason to expect injury. The last group needs further investigation, but pseudohemophilia, i. e., hemogenia, may play a rôle. Prophylaxis, diagnosis and therapy of the condition are all unsatisfactory.

ADAIR and POTTER, Chicago.

A CASE OF ANAEMIA NEONATORUM. K. KALBAK and T. K. WITH, Nord. med. tidskr. **12**:1921 (Nov. 21) 1936.

An infant born at full term, breast fed, weighing 3,400 Gm. at birth and having healthy parents, showed icterus neonatorum during the period from the second to the tenth day after birth. When the jaundice faded, the infant was found to be strikingly pale. The infant was first observed on the eleventh day. The hemoglobin was 48 per cent; the red blood corpuscles numbered 1,845,000 and the white blood cells 20,500 per cubic millimeter. There were 28 per cent immature myelocytes. There were 4,780 nucleated red cells per cubic millimeter. The sedimentation rate was 42. The anemia gradually improved without any treatment. At the age of 3 months the patient showed normal blood values: hemoglobin, 95 per cent; red blood corpuscles, 4,300,000; white blood cells, 6,100, with a normal qualitative blood picture. The nucleated red cells had disappeared when the infant was 1 month old. There was no decrease in the osmotic resistance of the blood corpuscles. The authors believe that the anemia was of hemolytic origin. They call attention to the sedimentation rate, which was very high at the first examination, gradually decreased but was still abnormal at the last examination, when the blood picture was normal.

WALLGREN, Göteborg, Sweden.

IDIOPATHIC MELAENA NEONATORUM. S. HAMMAR, Svenska läk.-tidning. **33**:1109 (July 24) 1936.

This report concerns seventy-six cases of melaena neonatorum recorded at the maternity hospital of Malmö, Sweden. The cases represented a frequency of three per thousand births. Among the patients there were as many boys as girls; among the mothers there were as many primiparas as multiparas. All except three infants were born at full term. The first symptoms were observed during the second and third day in 50 per cent of the patients and as late as on the fifth day in a few. Thirty per cent of the children had hematemesis. In the period from 1915 to 1921 there were twenty such patients, eight of whom died; in the period from 1922 to 1929, during which intramuscular injections of blood were used, seven of thirty such patients (23 per cent) died. From 1929 on, the children were treated with transfusions of blood (20 cc.) into the longitudinal sinus, and since then three of twenty-six (12 per cent) have succumbed.

WALLGREN, Göteborg, Sweden.

AT WHICH DEGREE OF DEVELOPMENT MAY A NEW-BORN HUMAN BEING BE CERTIFIED AS A CHILD? O. GRÖNÉ, Svenska läk.-tidning. **33**:1505 (Oct. 16) 1936.

After quoting opinions held by different noteworthy authors and criticizing the present valid definition in Sweden, Grönè suggests the following definitions: A child in the meaning of the law is any new-born dead or living infant which is at least 35 cm. in length or any new-born infant less than 35 cm. in length that has lived and breathed after birth.

WALLGREN, Göteborg, Sweden.

ANEMIA IN A NEW-BORN INFANT. E. GORTER, Nederl. tijdschr. v. geneesk. **79**:5620 (Dec. 7) 1936.

This is a description of a probable case of severe jaundice of the new-born without erythroblastemia, followed by hyperchromic anemia. Repeated transfusions and intramuscular injections of blood may have contributed to the recovery.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

RECENT EXPERIENCES IN SCARLET FEVER CONTROL. J. P. KOEHLER, Am. J. Pub. Health **25**:1359 (Dec.) 1935.

Koehler reports his extensive experience in the control of scarlet fever in Milwaukee. Group immunization was practiced in certain schools. Five doses of toxin were given at weekly intervals as recommended by the Dicks. Of 17,500 children given preliminary Dick tests, 66 per cent showed positive reactions. Of 6,000 children each of whom received 5 doses of toxin, 93.5 per cent showed a reversal of their reactions to negative. Severe reactions occurred in 3 per cent of the children, moderate reactions in 15 per cent, mild in 16 per cent and local reactions in 23 per cent; no reactions occurred in 43 per cent. In about 20 per cent of the children a rash developed after the second, third or fourth injection. The incidence of scarlet fever in completely immunized children was 2.3 per thousand, while in the elementary school population the incidence was approximately 60 per thousand. Children having only 2 doses of toxin had an incidence of 15 per thousand. Immunization is both effective and safe in controlling scarlet fever. Since many patients remain carriers after release from quarantine, this measure is of uncertain value. Quarantine of entire families is probably responsible for additional cases of scarlet fever. Nose and throat cultures for the control of carriers may be of value in prevention.

Strict isolation of all children under 7 years of age for six weeks during an epidemic of scarlet fever reduces the number of cases of scarlet fever and aids in control of other contagious diseases. Permanent control depends on the percentage of persons who have been made immune by the epidemic and by active immunization. Active immunization against scarlet fever is of definite value in prevention and should be widely practiced.

MCBRYDE, Durham, N. C.

PROGRESS REPORT ON PERTUSSIS IMMUNIZATION. P. KENDRICK and G. ELDERING, Am. J. Pub. Health **26**:8 (Jan.) 1936.

Using a vaccine somewhat similar to the one reported by Sauer, the authors found that only four of sixty children exposed to pertussis contracted the disease (dose, from 1,500,000 to 7,500,000 organisms). Sixty-three of eighty-four of the controls who were exposed contracted the disease. Those who received vaccine had mild pertussis, while most of the controls had typical or severe attacks.

MCBRYDE, Durham, N. C.

POLIOMYELITIS IN NORTH CAROLINA IN 1935. C. V. REYNOLDS and J. C. KNOX, Am. J. Pub. Health **26**:95 (Feb.) 1936.

In the five years before 1935 the average annual number of cases of poliomyelitis in North Carolina was 73. From January through October 1935, 641 cases were reported, mainly from the east central section of the state. The attack rate was 19.62 per hundred thousand, and the mortality was 9 per cent. The epidemic began in May, reached its height in June and July and had entirely subsided before October. Children of from 4 to 9 years were more often attacked. The attack rate per hundred thousand among white persons was 21.48, among Negroes 13.5 and among Indians 84. In Greensboro 300 children were vaccinated with the Park-Brodie vaccine, and no poliomyelitis developed in either the control or the vaccinated group. Six per cent of the vaccinations resulted in local abscesses, 12 per cent in nodules at the sites of vaccination and 12 per cent in medium-sized indurations.

MCBRYDE, Durham, N. C.

POLIOMYELITIS IN VIRGINIA DURING 1935. I. C. RIGGIN, Am. J. Pub. Health. **26**:98 (Feb.) 1936.

Poliomyelitis occurred in 674 persons in Virginia before November 1935. The paralytic form of the disease appeared in southern Virginia in June and gradually

spread northward, apparently along the routes of travel, but it reached epidemic proportions in only a few counties. The peak was reached about July 20. About a week later a wave of the nonparalytic form of the disease appeared in several counties. With the change in clinical type the distribution as to age changed markedly; 67.5 per cent of the paralyzed patients were under 10 years of age, while only 45.7 per cent of the nonparalyzed ones were under that age. The peak of the incidence of the nonparalytic form was not reached until about two weeks after the peak of the incidence of the paralytic form.

McBryde, Durham, N. C.

Anterior Poliomyelitis in Kentucky During 1935. A. T. McCormack and F. W. Caudill, Am. J. Pub. Health **26**:101 (Feb.) 1936.

Kentucky has from 20 to 40 cases of poliomyelitis annually in interepidemic years. In 1934, 118 cases were reported, 90 per cent of these occurring in the early summer and fall. Between July 1 and November 1936, 300 cases were reported. The mortality was 8.3 per cent, and 67 per cent of those recovering showed paralysis of some degree. Ninety-one per cent of the cases were in white children. The greatest incidence was in children under 5 years of age.

McBryde, Durham, N. C.

Poliomyelitis in Charlottesville, Virginia, and in the Adjacent County of Albemarle. W. W. Waddell Jr. and C. W. Purcell, Am. J. Pub. Health **26**:104 (Feb.) 1936.

During 1935 poliomyelitis was reported in 101 patients (73 children and 38 adults). The authors stress the importance of recognizing the nonparalytic, mild forms of the disease. They believe that the disease affected at least 1,500 persons in their community. The spinal fluid universally showed an increase in the protein content, but 39 patients in whom lumbar puncture was done within thirty-six hours after the appearance of acute illness showed less than 12 cells. The cell counts varied from 0 to 1,480, with an average of 155 cells for all those in whose spinal fluid cellular increases were shown. The diagnosis was made on the basis of clinical symptoms and signs plus the increase in protein in the spinal fluid. Headache was present in 74.7 per cent of the cases, vomiting in 55.9 per cent, fever in 54 per cent, change in reflexes in 47.8 per cent, pain and stiffness of the neck and back in 37.9 per cent and muscle weakness, abdominal pain and listlessness or drowsiness in 21.6, 18 and 15.3 per cent, respectively.

McBryde, Durham, N. C.

Immunity to Virus Diseases, with Particular Reference to Poliomyelitis. T. M. Rivers, Am. J. Pub. Health **26**:136 (Feb.) 1936.

Rivers doubts that inactive virus, even in large doses, causes more than temporary immunity. Permanent immunity following virus infections may be due to protracted intracellular sojourn of virus that is active, though it is not capable of spreading the disease. The patient becomes immune not because of antibodies present but because of recovery from a natural infection, as indicated by the presence of antibodies. Animals artificially immunized to poliomyelitis may have neutralizing antibodies without being resistant to the infection. Kolmer's poliomyelitis vaccine is said to be attenuated by passage through monkeys and by addition of chemicals. There is no evidence to show that poliomyelitis virus which has passed through monkeys is less infectious for man. Chemical attenuation is equivalent to dilution, and though the period of incubation is prolonged, the virus recovered from the sick animal is fully virulent. Few children are highly susceptible to poliomyelitis; so it is plausible to believe that those who contract the disease after one or two doses of Kolmer's vaccine were the ones who were most susceptible to the disease and who could not resist the active virus in the vaccine.

Brodie's vaccine is inactive poliomyelitis virus, and the favorable results depend on his ability to titrate accurately a paralyzing dose. Other workers have been able to find little if any protection with similar vaccines. As now prepared it is reasonably safe but ineffective.

McBryde, Durham, N. C.

Ocular Complications of Cerebrospinal Meningitis. E. B. Dunphy, Arch. Ophth. **15**:118 (Jan.) 1936.

This article is an ophthalmologic review of the literature on cerebrospinal meningitis, from the time it was first described, in 1805, by Vieusseaux and Matthey. The uveal tract and the retina are both involved at times. Apparently, the infecting organism is conveyed to the eye by way of the blood stream and not by direct spread from the meninges. In almost all cases the ocular inflammation begins during the stage of bacteremia, though later involvement of the eyeball may occur, owing to septic emboli. Collins and Mayou examined an eye with this complication pathologically and observed an embolus lodged in the ciliary body. The organism has been demonstrated within the eyeball on several occasions. Axenfeld cultivated it from an eye post mortem. McKee demonstrated it in the anterior chamber post mortem, and Weakley aspirated pus from the anterior chamber during the development of uveitis and from it grew a pure culture of the meningococcus.

Pathologic changes in the conjunctiva have long been recognized as a complication of epidemic meningitis. McKee made careful bacteriologic studies in six cases and in two cases obtained a pure culture of the meningococcus. Occasionally the meningococcus has been noted in the eyes of a patient not ill with epidemic meningitis. This led McKee to suggest that the eye might be a portal of entry for the infection. The cornea is not frequently involved. Parenchymatous keratitis has been observed. Corneal ulcers have been reported by several observers.

Pupillary abnormalities have been frequent. Dilatation and fixation of the pupils have occurred, each of which disappeared after subsidence of the infection. Inequality of the pupils has been observed. Hippus has occurred in a large number of cases, and in several instances there has been complete absence of the light reflex. Paralytic convergent strabismus has been found infrequently. Nystagmus is rare; in three of the seven instances in which it was noted it was vertical, and in one, rotary. It is a grave prognostic sign.

Optic neuritis is not infrequent, but papilledema is rare. True optic neuritis has been reported in from 4 to 18 per cent of cases, while papilledema was observed in only one instance. Three cases of retrobulbar neuritis have been reported in the literature; the patients were completely blind, without ophthalmoscopic lesions. In one of these cases autopsy was performed, but the cause of the blindness was not determined. Lewis, who discussed this, expressed the belief that in such instances the cause must be a lesion anterior to the primary optic centers—probably intense neuritis at the chiasm. He suggested that if the blindness is cortical one would expect retention of pupillary reactions.

Complete blindness has been noted as an early manifestation in infants. It is due not so much to optic neuritis as to an overwheming toxic impairment of the higher visual centers. In these cases the pupils remain active, though sluggish, and sight has been restored in many instances.

Spaeth, Philadelphia. [Arch. Neurol. & Psychiat.]

Labyrinthitis Secondary to Meningococcic Meningitis. Joseph G. Druss, Arch. Otolaryng. **24**:19 (July) 1936.

This report is based on the histologic study of sections of the temporal bone which revealed early as well as late pathologic changes of the labyrinth as a result of meningococcic meningitis. This extension usually takes place along preexisting routes or by way of the blood stream. Four cases of early changes and one in

which late changes were found are cited and discussed. The severity of the inflammation is responsible for the extent of the reparative processes, and formation of new bone plays an important part in the healing process. This causes occlusion of the semicircular canals, the cochlea and finally the vestibule, and the impairment of hearing is therefore progressive. Early treatment administered by way of the cerebrospinal fluid and the blood stream is advocated.

GREENWOOD, Chicago.

POLIOMYELITIS: DIAGNOSIS AND TREATMENT. THEODORE MELNICK, Arch. Pediat. **53**:433 (July) 1936.

The subject of acute anterior poliomyelitis is reviewed. Melnick encourages the use of convalescent serum or adult whole blood early in the course of the disease.

The discrepancies in the clinical results following the use of serum are due to several variables: (1) lack of a satisfactory method of determining the potency of the serum, so that the dose cannot be expressed in general terms, (2) variations in degree of severity of epidemics in different localities, (3) inclusion of unrecognized cases of mild involvement and (4) discrimination in time in early and late diagnosis.

ORR, Buffalo.

SCARLET FEVER TODAY. EDWARD L. BAUER, M. Clin. North America **20**:307 (July) 1936.

In a lucid discussion of the clinical and therapeutic aspects of scarlet fever Bauer attempts to evaluate the worth of serum therapy, active and passive immunization, the Dick test and the blanching test. With respect to these newer procedures, he confesses that the enthusiasm which once possessed him has waned and that a morbid pessimism has taken its place. Streptococcus haemolyticus scarlatinae has several strains, and the toxins produced by all strains are not identical. His suspicion that the Dick test is not a true measure of immunity to the disease was strengthened when he obtained positive reactions in 30 per cent of a group of children three years after bona fide attacks of scarlet fever. The therapeutic use of the Dick antitoxin may result in the prompt disappearance of all symptoms, but no marked reduction in complications has been proved to follow its use. Also, the frequent occurrence of severe serum reactions and anaphylactic phenomena discourage its use in all save severe cases. Bauer's experiences with active and passive immunization have been equally disappointing, and he has abandoned their use. He also believes that the blanching test will give inaccurate results when antitoxin is used instead of convalescent serum. He is convinced that in this branch of the study of scarlet fever it is necessary to lay a new foundation and that to this end all patients should be waived and the subject turned over to the laboratories, so that the bacteriologist and serologist may have complete freedom for investigation.

In summary, he proposes six cardinal points of attack on the disease: (1) more comprehensive and intimate study of its clinical aspects, (2) more complete isolation of patients, (3) longer periods of confinement to bed and more liberal management of diet, (4) more modern and radical management of complications, particularly surgical, (5) more careful and more reasonable consideration of release from quarantine and (6) liberation from commercialism of the bacteriologic and serologic studies necessary for the evolution of true prophylaxis and specific cure for the disease.

EUGENE SMITH, Ogden, Utah.

ACUTE APPENDICITIS AND MEASLES. H. W. HUDSON JR. and C. KRAKOWER, New England J. Med. **215**:59 (July 9) 1936.

To thirty-one instances of measles and appendicitis reported in the literature, nine are added. Regardless of whether measles is an etiologic factor in the

development of appendicitis, it is established that the two may coexist. If the signs of appendicitis are demonstrated, operation is indicated despite the presence of measles.

In the three cases the appearance of the exanthem and a complaint of abdominal pain were noted on the same day. In one case acute appendicitis occurred on the first day of illness and three days before the rash was noted. In the remaining four cases, the onset of abdominal symptoms was noted four, two, four and seven days, respectively, after the eruption was noted.

In another patient, not seen but of whom the authors had personal knowledge, abdominal symptoms and signs were present the day before the rash, but as Koplik spots, leukopenia and cough were noted, operation was deferred. Two days later there were signs of peritonitis, and operation was performed. Pneumonia developed four days after operation, and death ensued. The authors' patients recovered.

GENGENBACH, Denver.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **51**:1605 (Nov. 20) 1936.

During the period from Oct. 4 to 31, 1936, the incidence of poliomyelitis in the country as a whole dropped slightly. An exception was Oklahoma, with 31 new cases. With the exception of last year, the current incidence was the highest since 1931. The number of cases of scarlet fever rose to 10,000, but this is only 60 per cent of the incidence of the last three years. There was also an increase in diphtheria, measles and influenza, but the figures are not as high as for the usual seasonal incidence. The mortality from all causes was 11.8 per thousand, which is higher than that of the preceding three years.

SANFORD, Chicago.

MENINGOCOCCUS MENINGITIS: TREATMENT OF A CASE WITH MENINGOCOCCUS ANTITOXIN (FERRY) WITH RECOVERY. G. R. MAXWELL and R. S. SPRAY, West Virginia M. J. **32**:319 (July) 1936.

A boy 5 months old had meningococcic meningitis, the presence of meningococci of type III being confirmed by cultures.

Six doses of Ferry's meningococcus antigen were given, totaling 60,000 units. Of this antitoxin, 10,000 units was given intraspinally and 50,000 intramuscularly. Recovery was complete in thirty-four days. The condition was complicated by bronchopneumonia.

SHAWKEY, Charleston, W. Va.

A CASE OF CONCURRENT DIPHTHERIA AND VARICELLA WITH HEMORRHAGIC FEATURES. J. W. HEALY, Brit. J. Child. Dis. **33**:201 (July-Sept.) 1936.

A girl of about 6 years was admitted to the hospital with what appeared to be advanced nasopharyngeal diphtheria. Her condition was very toxic. Large doses of diphtheria antitoxin were given both intravenously and intramuscularly. On the day following admission lesions of varicella were noticed, the majority being hemorrhagic. Petechiae appeared in the clavicular and cervical regions and over the flanks and groins. The varicella eruption retrogressed, but the heart became dilated and heart block developed. She died on the ninth day after admission.

LANGMANN, New York.

TREATMENT OF ERYSIPELAS WITH ULTRA-VIOLET LIGHT. N. E. TITUS, Brit. J. Phys. Med. **11**:104 (Oct.) 1936.

Good results in the treatment of erysipelas with ultraviolet rays are reported. The use of a large initial dose, eighteen to twenty times the erythema dose for an adult and ten to twenty times the erythema dose for a child, is recommended.

HARTMAN, Cleveland.

EPIDEMIC POLIOMYELITIS. ARTHUR MACNALTY, Brit. M. J. **2**:57 (July 11) 1936.

This is a lecture delivered by MacNalty at the Royal United Services Institution in London on March 19, 1936, and is a general survey of the international investigation of epidemic poliomyelitis. It does not lend itself to abstracting, and it contains practically nothing new. ROYSTER, University, Va.

CONSERVATIVE TREATMENT OF LARYNGEAL DIPHTHERIA. JAMES HAY CLARKE, Brit. M. J. **2**:66 (July 11) 1936.

Clarke reports his experience with laryngeal diphtheria in a hospital for the treatment of infectious diseases. ROYSTER, University, Va.

HERPES ZOSTER AND VARICELLA. H. MALLINSON, Brit. M. J. **2**:1197 (Dec. 12) 1936.

In reporting two cases Mallinson makes a brief statement concerning the theories as to the possible relationship between the virus of herpes zoster and that of varicella. In one case the patient had an eruption of herpes zoster and seven days later severe typical varicella. In the second case the patient had typical varicella; fourteen days after this a son came down with typical varicella and fourteen days later the husband. In the author's mind is a question whether these were incidental infections or variant manifestations of the same virus.

ROYSTER, University, Va.

THE DIFFERENT FORMS OF CORYNEBACTERIUM DIPHTHERIAE AND THEIR SIGNIFICANCE. W. MAIR, J. Path. & Bact. **42**:635, 1936.

The so-called barred or intermediate forms of Corynebacterium diphtheriae all belong to one serologic type. More than 80 per cent of the strains of C. diphtheriae found in definite cases of diphtheria in the London area belong to one or the other of two serologic types: the barred form (F) and the starch-fermenting type (A). Forty-five per cent of the strains of C. diphtheriae found in convalescents and carriers and in persons with conditions the clinical diagnosis of which is doubtful are of the mitis type. Practically all the nontoxigenic strains of C. diphtheriae belong to this mitis type. The different forms of C. diphtheriae may change in artificial culture from one to another.

FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

TITRATION OF VACCINIA VIRUS ON THE CHORIO-ALLANTOIC MEMBRANE OF THE CHICK EMBRYO. E. V. KEOGH, J. Path. & Bact. **43**:441, 1936.

Any suspension of the virus of vaccinia, inoculated in suitable dilutions, will produce discrete lesions on the chorio-allantoic membrane of the developing embryo of the chick. The titer of a vaccinial suspension obtained by enumeration of such lesions corresponds to that found by intradermal inoculation in the rabbit. Immune serums can be titrated in respect to their inactivating properties by the percental reduction effected in the number of such lesions. By this quantitative technic it is shown that the inactivating principle of immune serum combines with the particles of virus in vitro and that the union is partly dissociated by simple dilution. The percental inactivation of the virus of vaccinia effected by immune serum is independent of the concentration of the virus within the experimental range. FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

THE IN VITRO CULTIVATION OF THE FILTERABLE VIRUSES, WITH PARTICULAR REFERENCE TO VACCINE. R. A. ALEXANDER, South African M. J. **10**:467 (July 11) 1936.

The present status of the subject of in vitro cultivation of viruses is briefly reviewed. Alexander is of the opinion that in the near future, at least in the case of vaccinia, cultured virus will replace the bacteriologically unsavory calf lymph

now in use for general routine immunization. Of the two methods—the tissue culture method and the chick embryo method—the latter is favored by the author as the simpler, the more uniform and the less open to error and accident.

GONCE, Madison, Wis.

MENINGITIS IN ASSOCIATION WITH MUMPS. MICHAEL CAMNER and MARIE CAMNER, Bull. Soc. de pédiat. de Iasi **6**:81 (Oct.-Dec.) 1935.

Two cases of meningitis associated with mumps are reported. In both, there was an abrupt onset of the nervous symptoms before any swelling of the parotid gland was noted. The spinal fluid was clear but showed a marked lymphocytic reaction (on one occasion 345 lymphocytes per cubic millimeter). The Nonne-Appelt reaction was slightly positive. There was no pellicle formation.

LESLIE, Evanston, Ill.

MENINGOCOCCIC MENINGITIS WITH OCULAR COMPLICATIONS. S. GRAÇOSKY, C. HURMUZACHE and E. TRIANDAF, Bull. Soc. de pédiat. de Iasi **7**:28 (Jan.-March) 1936.

An infant 9 months of age showed, first, typical meningitis, from which there was rapid recovery, and, second, an infection in both eyes. There were uveitis of the left eye and inflammation of the optic nerve in the right eye. The prognosis for vision was grave.

LESLIE, Evanston, Ill.

VALUE OF SERUM THERAPY IN HEINE-MEDIN DISEASE. P. GIRAUD and JOUVE, Rev. franç. de pédiat. **12**:57, 1936.

Giraud and Jouve report their experience with sixteen cases of poliomyelitis during an epidemic. Most of the patients they did not see until after the onset of some paralysis. In treatment, they employed a serum prepared by immunizing a horse according to the method of Pettit. This was given subcutaneously or intramuscularly in doses of from 80 to 300 cc. They admit that it is difficult to judge the benefit derived from this serum but feel that it prevented further progress of the disease, particularly disease of the ascending bulbar type. In the one case in which the serum was given before the onset of any paralysis there were no sequelae. There were no deaths.

LESLIE, Evanston, Ill.

COMPLICATIONS INVOLVING THE RESPIRATORY TRACT IN TYPHOID. S. GATTO, Clin. pediat. **18**:414 (July) 1936.

Gatto studied the incidence of complications involving the respiratory tract among nearly 1,200 children with typhoid or paratyphoid who had been treated in the Pediatric Clinic of the University of Bologna in the past thirty years. There had been no complication or only minimal involvement of the bronchi in 28.9 per cent, definite involvement of the bronchi in 56.5 per cent, bronchopulmonary complication in 13.4 per cent and pleuropulmonary complication in 12.2 per cent. He notes the frequency of respiratory involvement among children as contrasted with adults and comments on the differences in the course and prognosis as influenced by the location of the complication. The frequent occurrence of bronchitis of spastic or asthmatic type in children was especially noteworthy. As instances of rare complications, he reports one case of pulmonary abscess, two of pulmonary gangrene and three of spontaneous pneumothorax.

DOOLEY, New York.

HISTOLOGY OF THE CONJUNCTIVAL MUCOSA IN MEASLES DURING THE INCUBATION PERIOD. A. ROBLES, Riv. di clin. pediat. **34**:991 (Nov.) 1936.

Biopsies of the conjunctivae of nine children, of whom seven had measles, were made. A mesenchymal growth due to an inflammatory stimulus was

observed. This stimulus may have been the virus of measles. A similar growth is noted in other conditions on rare occasions and may be due to a tissue reaction to a similar but different stimulus.

HIGGINS, Boston.

INTRADERMAL VACCINATION FOR SMALLPOX. J. F. FRANCO, Rev. mex. de puericultura **5**:925 (Dec.) 1935.

Franco concludes that intradermal vaccination for smallpox is inferior to the method in regular use. It is more complicated. The absence of a scar produces difficulties in obtaining a certificate of vaccination. It is harder to tell whether there is a "take" or not. Last, there is more pain associated with it. He does not recommend it.

HERRON, Spokane, Wash.

IMMUNIZATION OF HYPOPHYSECTOMIZED DOGS WITH DIPHTHERIA ANTITOXIN. A. H. ROFFO and A. E. ROFFO JR., Rev. Soc. argent. de biol. **11**:107 (May) 1935.

Seven hypophysectomized and five normal dogs were used. One injection of diphtheria antitoxin was given per week, the doses being increased from 1 to 80 cc. Every two weeks a sample of blood was taken and analyzed. Diphtheria antitoxin increased with great rapidity in the serum of the hypophysectomized dogs as compared with the normal dogs.

HERRON, Spokane, Wash.

PRIMARY DIPHTHERIA OF THE EXTERNAL GENITALIA OF YOUNG GIRLS. A. D. JAWOROWSKAJA, Dermat. Wchnschr. **102**:312 (March 14) 1936.

The literature in regard to primary diphtheria of the genitalia is briefly discussed, and four cases observed by the author are described. He points out that local therapy as well as general treatment is required.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

A PECULIAR AND HITHERTO UNREPORTED PHENOMENON OBSERVED IN CHILDREN IMMUNIZED AGAINST MEASLES BY INJECTIONS OF NORMAL BLOOD. FRITZ GOEBEL, Kinderärztl. Praxis **7**:293 (July) 1936.

In four children who, soon after exposure to measles, had received from 20 to 45 cc. of whole blood obtained from adults, Goebel observed severe swelling and tenderness at the site of injection, accompanied by fever, the temperature being 38 to 39 C. (100.4 to 102.2 F.). The swelling and tenderness appeared at the time that measles prodromes would otherwise have become apparent, that is, about the tenth to the eleventh day of incubation, or from six to eight days after the injection of the blood. The local symptoms subsided entirely in one or two days. Goebel expresses the belief that a virus-antivirus reaction is the cause of this phenomenon.

HEYMANN, Cleveland.

MEASLES AND TUBERCULOSIS. PAUL SVASTITS, Monatschr. f. Kinderh. **66**:149 (July) 1936.

In the extensive measles epidemic of 1935 in Hungary, Svastits studied the effect on children with latent tuberculosis. Among seventy who reacted positively to tuberculin, latent tuberculosis was activated in 7 (10 per cent). He concludes that there is every reason for not disregarding the old fear of measles in patients with latent tuberculosis and for making every effort to protect them from measles.

GERSTLEY, Chicago.

SUSCEPTIBILITY OF CHILDREN WITH SCARLET FEVER TO DIPHTHERIA. Z. TEVELI, Orvosi hetil. **80**:1065 (Nov. 7) 1936.

It occurs very often in departments of scarlet fever that the children get diphtheria. Some authors believe that in the presence of scarlet fever the anti-

toxin of the blood diminishes. Park and Zingher found positive Schick reactions among children who had recovered from scarlet fever much more often (57 per cent) than among those who had not had the disease (24 per cent). In fourteen cases of scarlet fever Teveli systematically examined the behavior of the antitoxin content of the blood against diphtheria (usually three examinations were made on every child) and found that the antitoxin content may show some vacillation but that this is not the rule. He thinks that mixed infections occur not because the antitoxin content has lessened but because in these departments there are many diphtheria bacilli which can more easily penetrate tonsils weakened by scarlet fever. The mixed infections are, on the whole, not severe just because the antitoxin content is not diminished.

GÖTTCHE, Budapest, Hungary.

IMMUNITY AGAINST DIPHTHERIA AND THE ANTITOXIN CONTENT OF THE BLOOD. Z. TEVELI and K. FEJES, Orvosi hetil. **80**:1093 (Nov. 14) 1936.

Teveli and Fejes infected the corneas of seventy-three guinea-pigs. Part of these were immunized against diphtheria with anatoxin. Another part were not. The course of diphtheria was milder in the immunized than in the nonimmunized animals, but diphtheria developed also in animals with a high antitoxin content. Severe diphtheria developed mostly among immunized animals whose blood showed only little antitoxin. On the whole, the local procedure and the situation in its entirety depend on the antitoxin content of the blood. Whereas more than half of the nonimmunized animals died of the infection, all the immunized ones except two lived. The minimal antitoxin content may have some power of immunization, but the antitoxin content is not the only factor in the problem of immunity against diphtheria.

GÖTTCHE, Budapest, Hungary.

CORTICAL FORM OF POLIOMYELITIS. P. KISS and I. FÉNYES, Orvosi hetil. **80**: 1141 (Nov. 28) 1936.

These authors think that the pathologic picture described by von Strümpell and Marie is not identical with infantile paralysis. There are many great epidemics of poliomyelitis in which this pathologic picture could not be observed. In a case reported by Rothmann, in which the clinical symptoms of Strümpell-Marie were shown, the blood serum did not neutralize the virus of poliomyelitis and the histologic examination showed great bleeding in the brain and extensive softenings of both the cortical and the white matter. Poliomyelitis has a cortical form, but it differs from the clinical picture described by von Strümpell and Marie. The experiments of Pette, Demme and Környei and the histologic examinations of Horányi showed that in every case of infantile paralysis the gyrus centralis anterior on each side of the brain is affected. In three cases of paralysis of the legs the patellar reflexes were increased, and the Babinski sign was present on each side. The authors think that the increase in the patellar reflexes and the bilateral positive Babinski sign are caused by bilateral injury of the gyrus centralis anterior.

GÖTTCHE, Budapest, Hungary.

TREATMENT OF PERTUSSIS WITH VITAMIN C. T. OTANI, Orient. J. Dis. Infants **20**:1 (July 11) 1936.

Otani found that vitamin C has an effect of regression on the growth of Bacillus pertussis in vitro and that the toxicity of the organism is greatly reduced when the culture medium contains a large amount of vitamin C. The organism thus cultured produces on injection, instead of absolute lymphocytosis, leukocytosis with neutrophilia. Although in titer of agglutination and complement-binding reaction the two strains of pertussis bacilli are practically identical, the strain grown on medium containing vitamin C has a greater power for the production of immunity. On the basis of these experimental observations Otani treated eighty-one children who had whooping cough with large amounts of vitamin C. Thirty-four responded remarkably well, thirty-two were but moderately benefited, and fifteen were considered unaffected.

KATO, Chicago.

A New Method for the Diagnosis and Vaccinal Treatment of Whooping Cough. E. J. Berman and E. N. Podwalny. Acta pædiat. **19**:232, 1936.

The authors have worked out the technic of a skin test which is helpful in establishing a diagnosis of whooping cough. They employed a solution of the toxin elaborated by the Bordet-Gengou bacillus, prepared by the Metchnikow Institute of Bacteriology in Moscow according to the method of Huntoon. One tenth of a cubic centimeter of the solution was injected intracutaneously. Two types of reaction were observed. The first, which was urticarial in character, appeared within five to twenty minutes after the injection; this is designated "allergic." The second type of reaction, which is called "positive," appeared between six and eight hours after the injection and lasted about twenty-four hours; it consisted of erythema without wheal or vesiculation. The first type of reaction was given most frequently by patients who had recently been vaccinated prophylactically, and with decreasing frequency by (a) those who had recently recovered from pertussis and (b) those who were still in the paroxysmal stage of the disease; it was also given by 21 per cent of patients who were not known to have had pertussis. The "positive" reaction, that is, the one which indicates complete or relative lack of immunity, was found in 76 per cent of 181 children who had never had whooping cough, 41 per cent of 53 children who had had the disease several months before, 23 per cent of 36 children during the course of the illness, and in 18 per cent of 19 children who had just recovered from the disease. The effect of prophylactic vaccination with the Bordet-Gengou bacillus was studied in 60 infants: before vaccination 71 per cent gave a "positive" reaction; 1 month after vaccination only 39 per cent showed this type of response.

Therapeutically, the authors tried a combined treatment which consisted of Bordet-Gengou vaccine and streptococcus vaccine; the latter contained both killed organisms and soluble toxin. The results which were obtained with this type of treatment were sufficiently encouraging to justify further trial.

McCune, New York.

Diphtheria of the Lips. L. van der Molen. Nederl. tijdschr. v. geneesk. **79**: 5753 (Dec. 14) 1935.

Van der Molen reports a case of primary diphtheria of the lips, complicated by paralysis of the neck muscles, in a boy of 3 years. Complete recovery took place.

van Creveld, Amsterdam, Netherlands.

Acute Infectious Diseases

The Diagnosis of Gonococcal Infections by the Cultural Method. Alice D. Leahy and Charles M. Carpenter, Am. J. Syph., Gonor. & Ven. Dis. **20**:347 (July) 1936.

The authors' summary, which follows, adequately outlines the method of procedure.

"1. A modification of McLeod's cultural method for the diagnosis of gonococcal infections is described. The method consists in making cultures on "chocolate" agar, prepared with a Douglas agar base, and incubating them at 34° C. and at 37° C. in an atmosphere of air reinforced approximately to 10 per cent in its carbon dioxide content. The oxydase test, employing a 1 per cent aqueous solution of dimethyl-para-phenylenediamine hydrochloride, is used to identify gonococcus colonies in mixed cultures.

"2. There were isolated by this technic 130 cultures of Neisseria gonorrhoeae, representing 43 per cent of the 302 specimens submitted for examination from 138 patients. The cultural method resulted in the discovery of 10 per cent more positive cases of gonococcal infections than did the smear method alone. This percentage is much higher when only specimens from the lower birth canal and from prostatic secretions are considered.

"3. The incubation of cultures in an atmosphere of air reinforced to approximately 10 per cent in its carbon dioxide content resulted in the isolation of 15 per cent more cultures of gonococci than were recovered from duplicate cultures incubated in air under conditions that were otherwise identical.

"4. The use of the oxydase test detected 21, or 14 per cent, of 146 cultures of N. gonorrhoeae that would have been reported negative had direct inspection alone been relied upon."

ROYSTER, University, Va.

STUDIES ON TETANUS TOXOID: III. ANTITOXIC RESPONSE IN GUINEA PIGS IMMUNIZED WITH TETANUS ALUM-PRECIPITATED TOXOID FOLLOWED BY TETANUS SPORES. F. G. JONES and W. A. JAMIESON, J. Bact. **32**:33 (July) 1936.

Jones and Jamieson open their paper with the question: "When an individual has been given one or more injections of tetanus toxoid and at a later date is injured and possibly infected with *Clostridium tetani,* what further precautions should be taken: (1) Administer antitoxin? (2) Give another injection of tetanus toxoid to accelerate the production of antitoxin? (3) Give no further treatment, depending on his present immunity to take care of the infection?"

The original idea in administering tetanus toxoid was to avoid the use of antitoxin. Using guinea-pigs the authors found that another injection of toxoid at the time of injury will quickly increase the antitoxin content twentyfold. They went further to ascertain whether a huge dose of tetanus spores accelerates the production of additional antitoxin and found that a massive dose of tetanus spores does not markedly accelerate the production of antitoxin in guinea-pigs that have been previously immunized with alum-precipitated tetanus toxoid.

STOESSER, Minneapolis.

SYMPOSIUM ON FEVERS OF OBSCURE ORIGIN IN CHILDHOOD. JOSEPH STOKES JR., MITCHELL I. RUBIN, CHARLES C. CHAPPLE, JOHN MCKENNEY MITCHELL and T. S. WILDER, M. Clin. North America **20**:3 (July) 1936.

As Stokes remarks in his introduction, difficulty in the diagnosis of obscure fever is often due not to lack of careful examination or to failure to analyze carefully signs and symptoms, but to the fact that the correct cause of the condition does not occur to the physician. The objectives, therefore, of this symposium are to present in reasonable order the names of a variety of conditions which might not readily occur to the practitioner and to review under each diagnosis a few facts of outstanding clinical importance. These are considered under the following heads:

Fevers due to infections of the upper respiratory tract.
Fevers of abdominal origin.
Fevers due to diseases of the urinary tract.
Fevers discussed from the standpoint of disease of the central nervous system.
Fevers due to miscellaneous conditions.

The practitioner will find in this symposium a comprehensive summary of the causes of obscure fever with which to refresh his memory when he is confronted with these puzzling conditions.

EUGENE SMITH, Ogden, Utah.

SUCCESSFUL TREATMENT OF BRUCELLA MENINGITIS WITH IMMUNE HUMAN SERUM: ISOLATION OF THE ORGANISM BY A MODIFIED CULTURAL METHOD. M. A. POSTON and D. T. SMITH, New England J. Med. **215**:369 (Aug. 27) 1936.

Brucella infection should be suspected in cases of atypical meningitis. Brucella meningitis can be treated with immune serum obtained from persons who have been actively immunized to brucella or possibly from persons convalescent from

the disease in the community whose blood serum is high in agglutinin for the specific organism isolated from the spinal fluid.

Patients who have no agglutinins for brucellas in their blood after recovery should be immunized by autogenous vaccine therapy (their own organism being used) to prevent a recurrence of the infection.

Two cases of brucella meningitis are discussed in which the patients recovered rapidly and apparently completely after intrathecal treatment with fresh human immune serum.

GENGENBACH, Denver.

EPIDEMIC CATARRHAL JAUNDICE, WITH SPECIAL REFERENCE TO ITS EPIDEMIOLOGY. W. N. PICKLES, Brit. J. Child. Dis. **33**:192 (July-Sept.) 1936.

Epidemic catarrhal jaundice is a nonspirochetal infectious hepatitis, whereas Weil's disease is due to a spirochete. In addition, there are marked clinical and epidemiologic differences.

Unlike the spirochetal form, the disease appears to spread from person to person, probably by droplet infection. It affects mainly children. The incubation period is thought to be approximately a month. The etiologic agent of this disease has not been discovered.

LANGMANN, New York.

AN OUTBREAK OF TICK-BITE FEVER. J. H. S. GEAR and C. BEVAN, South African M. J. **10**:485 (July 11) 1936.

Gear and Bevan traced an outbreak of tick fever to the manual deticking of dogs and the crushing of the ticks so removed between the fingers.

GONCE, Madison, Wis.

THROMBO-ARTERITIS OCCURRING IN THE COURSE OF TYPHOID FEVER. C. HURMUZACHE and E. LUCINESCU, Bull. Soc. de pédiat. de Iasi **7**:15 (Jan.-March) 1936.

Several weeks after the onset of typhoid fever in a boy 9 years of age there was a sudden development of left hemiplegia. This was followed several days later by ischemia of the right leg. It was thought that the ischemia was due to an embolus, and the femoral artery was resected and an infected thrombus found. The blood culture was positive for Eberthella typhosa. It was still open to question whether both processes were embolic or were in the nature of obliterating endarteritis.

LESLIE, Evanston, Ill.

MALIGNANT FORM OF RHEUMATIC FEVER IN CHILDREN. H. GRENET, Gaz. d. hôp. **109**:1624 (Nov. 25) 1936.

General malaise, anorexia, pallor and dyspnea for from seven to fifteen days constitute the prodromal phase. Salicylates lower the temperature somewhat but do not bring it down to normal. The pulse is always rapid, and usually the diuresis is very scant. Nonprotein nitrogen may be as high as 85 per cent without recognizable renal lesions. The prognosis depends on the severity of the myocardial lesions rather than on the intensity of the arthritic symptoms. Pulmonary stasis and pleural effusions are not infrequent complications. The spleen is enlarged in 50 per cent of the cases. Grenet could not culture Streptococcus in his cases. The course is continuous progression, leading to death in a few years.

As therapy salicylates and long absolute rest are recommended.

KAJDI, Baltimore.

HELMINTHIASIS IN CHILDREN. E. E. KATZMANN, Rev. franç. de pédiat. **12**:75, 1936.

This study was carried on in Minsk, White Russia. Of 2,200 children examined, 1,984 were found to have intestinal worms, and 95 per cent of these harbored

Ascaris lumbricoides. Chief among the complaints were nausea, anorexia, vertigo, headache, weakness and abdominal pain. A strawberry appearance at the end of the tongue, described by Barvinsky, was noted in most instances. The gastric acidity, studied in 66 cases, was normal in 30, increased in 16 and diminished in 20. Excessive salivation was a prominent feature, which disappeared when the patient was rid of the worms. Education, improved hygiene and a pure water supply must be had if this state of widespread helminthiasis is to be improved.

LESLIE, Evanston, Ill.

STAPHYLOCOCCIC SEPSIS IN CHILDREN. G. SALVIOLI and G. MAZZETTI, Riv. di clin. pediat. **34**:961 (Nov.) 1936.

Two cases of acute septicemia and arthritis are reported. A boy of 9 was taken suddenly ill with a high fever and swelling of the right knee; later purulent pericarditis and an abscess of the left zygoma developed. The other child, a girl of 11, had a sudden onset of pain and swelling of the left hip; on the second day a scarlatiniform eruption appeared over the trunk and extremities, but with no involvement of the throat. The latter patient died one day later; a necropsy was performed.

In the blood cultures in each case Staphylococcus aureus was obtained. In neither child was a portal of entry for the infection apparent. The bacterial cultures were virulent for rabbits but not for mice. The bacteria seemed to localize in the joints of rabbits given intravenous injections; control observations, however, with cultures of Staphylococcus obtained from a parotid abscess of another patient showed similar localization in the joints.

HIGGINS, Boston.

A CHARACTERISTIC PULMONARY SYNDROME FROM MALARIA IN A BOY. A. BARCAGLIA, Riv. di clin. pediat. **34**:1011 (Nov.) 1936.

A boy 3½ years of age showed intermittent fever and, at the time of the fever, definite signs of confluent bronchopneumonia of the base of the left lung. The cause of the condition turned out to be tertian malaria, which responded to quinine therapy. The author suspects that the pulmonary signs in this case were of an anaphylactic origin.

HIGGINS, Boston.

KALA-AZAR CURED WITH UREA STIBAMINE. P. BUXÓ IZAGUIRRE, An. de pediat. **2**:84 (Feb.) 1935.

The author presents a case of kala-azar occurring in a young child in which treatment was by intravenous administration of urea stibamine (an antimony compound). The initial dose of 0.005 Gm. was increased rapidly, with daily injections, to 0.15 Gm.; then this dose was given three times a week. A total of 1.44 Gm. was given, and a complete cure was obtained.

HERRON, Spokane, Wash.

ROENTGEN DIAGNOSIS OF ASCARIS LUMBRICOIDES IN THE HUMAN ALIMENTARY TRACT. R. WIGAND, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:607 (Dec.) 1936.

Experimentally it was not possible to introduce the usual contrast mediums into the intestine of the ascarid, either by mouth or through osmosis. For this reason, the conclusion is drawn that the roentgen phenomenon which is diagnostic of the presence of ascarids is probably due to a filling defect produced by them or to a coat of contrast medium on the body of the worm.

MCCUNE, New York.

THE CARDIOVASCULAR SYSTEM DURING CONVALESCENCE FROM TYPHOID FEVER. F. D. GUREWITSCH, Monatschr. f. Kinderh. **64**:341, 1936.

Gurewitsch made a special study of the cardiovascular system in sixty-five children during convalescence from typhoid. Studies were made from three points of view: disturbances of the cardiac muscle, disturbances of rhythm and hypotonia. The usual methods of investigation were employed, such as noting the subjective symptoms of weakness, dyspnea and easy fatigability. Physical examination included the usual percussion and auscultation as well as roentgenograms and electrocardiograms. Hypotonia was diagnosed by observation of a maximum blood pressure below 90 mm. of mercury. This was present in the entire series.

Gurewitsch concludes that the average child should be kept at home for about twenty days after the temperature has become normal. If, however, at that time there are still any abnormal symptoms, he should be kept at home for one and one half months.

GERSTLEY, Chicago.

RELATION OF RHEUMATISM TO ALLERGY. C. KEIFFENHEIM, München. med. Wchnschr. **83**:1299 (Aug. 7) 1936.

Rheumatic arthritis has been considered by some investigators to be due to some food allergen. Good results have been reported from desensitizing with the offending substance. The author performed skin tests in one group of patients with rheumatic arthritis, in another group with arthrosis and neuralgia and in a third group not suffering from any nerve or joint symptoms. The tests were not strikingly different in any group. He also failed to find any decrease in the skin reactions after giving salicylates, amidopyrene or cinchophen. The conclusion reached is that rheumatic arthritis is not due to a food allergy.

BRAHDY, Mt. Vernon, N. Y.

DYSENTERY: ITS FORMS, AND PRINCIPLES OF TREATMENT. I. R. BRAUDE, Vrach. delo **19**:1051, 1936.

Braude believes that dysentery should be classified and differentiated not only according to the causative agents (forms of the Shiga-Kruse type and paradysentery) but, above all, according to the degrees of toxicity and the kinds of reactivity of the macro-organism, consideration being given also to the general state of the macro-organism as well as to the local manifestation of the disease as colitis.

On this basis he suggests the desirability of individualizing the treatment of dysentery. He believes in the effectiveness of bacteriophage and specific serotherapy in some cases as well as in the effectiveness of the symptomatic treatment, the laxative and the diets for dysentery.

BODER, Los Angeles.

TETANUS AFTER PROPHYLACTIC INJECTION OF SERUM. W. A. TIMMERMAN, Nederl. tijdschr. v. geneesk. **79**:5632 (Dec. 7) 1935.

Fatal tetanus developed after early and adequate treatment of a wound and prophylactic injection of serum. The problems which arise in the consideration of this case, such as the time of treatment after the accident and the quantity of serum to be injected, are discussed.

VAN CREVELD, Amsterdam, Netherlands.

THE DANGER OF PARATYPHOID FROM CONTACT WITH DUCKS. A. C. RUYS, Nederl. tijdschr. v. geneesk. **80**:3272 (July 11) 1936.

A child probably contracted salmonella infection from two little ducks with which she played. One of them died, and the other was a healthy carrier of Salmonella aertrycke. In several families insufficiently heated duck soup caused an outbreak of salmonella infection. In chicken broth which also caused an outbreak of paratyphoid B a strain of S. aertrycke could be isolated from the interior of the chicken's leg.

VAN CREVELD, Amsterdam, Netherlands.

Chronic Infectious Diseases

B C G Vaccination in Western Europe. C. Gregory Kayne, Am. Rev. Tuberc. **34**:10 (July) 1936.

Kayne gives a critical review of the work being done with B C G in western Europe based on his personal investigations. While it is true that B C G is not a *virus fixé* and under certain laboratory procedures it is possible to restore its virulence, this fact is no contraindication to its use in man provided the routine method of subculture does not have that effect. With certain of the methods at present in use it appears to become slowly more attenuated. In determining the extent and duration of immunity in vaccinated persons, three conditions are necessary: 1. The number of living bacilli in the emulsion should, as far as possible, be constant. 2. The greatest possible number of living bacilli in the vaccine administered should gain entrance to the tissues. 3. A positive reaction to tuberculin should be obtained, which, if the child has not been in contact with tuberculosis, is an indication that the tissues have reacted to the bacilli. Judged by these criteria, (1) B C G vaccination produces a partial immunity, which is likely to play an effective rôle only when it is combined with other methods of prophylaxis; (2) the duration of the immunity varies considerably but is generally between six and twelve months.

The essentials on which to base a rational application of B C G are:

1. The vaccine must be stable and of standard strength.

2. A suitable route of administration must be employed. The intracutaneous route seems to be the method of choice. The oral method, while perhaps too much condemned, is not to be relied on.

3. A dose of vaccine should be used which will produce hypersensitiveness to tuberculin as rapidly as possible with the least inconvenience.

4. Vaccinated children should not be in contact with tuberculous contagion until a positive tuberculin reaction is obtained.

5. Only children definitely risking contact with tuberculosis should be vaccinated.

Two facts with regard to B C G are emerging: It is harmless, and it is of some value, if used under certain conditions, as an adjunct to other methods of prophylaxis.

Eugene Smith, Ogden, Utah.

Antisyphilitic Treatment: Effect of Rest on the Results of Treatment and the General Benefit Derived from Therapy. M. E. Obermayer and S. William Becker, Arch. Dermat. & Syph. **34**:57 (July) 1936.

Since the advent of "chemical success" in the treatment of syphilis, the nonspecific aids have been laid aside. It is this point which Obermayer and Becker wish to emphasize. In their treatment of syphilitic patients they found the best results in those who worked nine hours or less, got eight hours of sleep at night, took an afternoon nap and had a vacation in some quiet place for a week or two in the year. There was in general in these patients a gain in weight and a feeling of "well being" after treatment was started, while in less fortunate patients, whose working hours were longer and who had less rest, the results were not as favorable. At the Mayo Clinic the patients are "hospitalized for one day after the administration of arsphenamine and rest during the remainder of the week." The results obtained are better than those in urban practice. The authors make the following statement: "The data gained from this study show sufficient beneficial effect of regular and restful living to warrant the statement that the physician who treats syphilis should emphasize to every patient under his care the paramount necessity of rest and relaxation for obtaining the most satisfactory results from antisyphilitic treatment."

Dulin, Iowa City.

NITROGEN METABOLISM IN ANEMIA DURING THE REGENERATION OF BLOOD. C. W. HEATH and F. H. L. TAYLOR, J. Clin. Investigation **15**:411 (July) 1936.

The effect of the regeneration of hemoglobin on the retention of nitrogen, on the plasma protein and nonprotein nitrogen and on the tissue nitrogen was studied in nine severely anemic adult patients. Under appropriate treatment, formation of hemoglobin was found to proceed even in the face of a negative nitrogen balance. The demand for nitrogen under these circumstances seemed to be supplied by tissue and plasma nitrogen.

GUEST, Cincinnati.

EXPERIMENTAL SYPHILITIC KERATITIS IN THE RABBIT. A. J. GELARIE, J. Infect. Dis. **59**:221 (Sept.-Oct.) 1936.

Syphilitic material injected into the anterior chamber of the eye and into the testicle of the rabbit simultaneously produces interstitial keratitis.

The spirochetes are apparently adapted to produce keratitis on serial passages of syphilitic corneas into the anterior chamber of the eye.

Interstitial keratitis is more suitable for the study of therapeutic effects than are testicular lesions.

TOOMEY, Cleveland.

FACTORS INFLUENCING THE DEVELOPMENT OF TUBERCULOUS INFECTION IN CHILDHOOD. A. S. JOHNSON, New England J. Med. **215**:239 (Aug. 6) 1936.

The group studied comprised 375 children under 16 years of age who were examined at the Health Department Tuberculosis Dispensary in Springfield, Mass. Of these, 218 gave a definite history of contact with persons known to have pulmonary tuberculosis; 157 children who had no history of such contact were presented for examination because of malnutrition, recurrent respiratory infections or vague apprehension on the part of the parent. The examination of each child included recording the age, sex, height, weight, temperature, tuberculous contacts, periods of exposure, cutaneous tuberculin reaction after forty-eight hours, taking an x-ray picture of the chest, and an appraisal of the domestic hygiene as a result of a personal investigation of the home. Of the children who had never been exposed to recognized tuberculosis, only 21 per cent showed positive cutaneous reactions, whereas 57 per cent of the contact children and 63 per cent of those exposed to sputum containing the bacilli had positive cutaneous reactions.

Sex appeared to have little bearing on susceptibility to tuberculous infection. Of the children exposed to a tuberculous father, 70 per cent had positive reactions, whereas only 53 per cent of those with a tuberculous mother had such reactions. The contact children who had been exposed chiefly during the first five years of life did not show the highest incidence of positive skin reactions. The second and third five year periods appeared to be associated with distinctly more vulnerability. On the other hand, of all the contact children having positive skin reactions, the highest percentage was found to have received their maximal exposure during the first five years of life. As might be expected, the longer the exposure the greater was the chance of infection.

So far as general characteristics were concerned no one age, sex, social or economic group could be identified as including the greater portion of infection. Twenty-three per cent of the children with positive reactions were underweight, and nearly 40 per cent of the underweight children had positive reactions. Approximately 25 per cent of all the children examined in the clinic were 10 per cent or more underweight.

GENGENBACH, Denver.

MUCOCUTANEOUS SYPHILIS (BEJEL) IN SYRIA—THE RESULTS OF DARK FIELD EXAMINATION. E. H. HUDSON, New England J. Med. **215**:392 (Aug. 27) 1936.

Bejel is the name given by the Arabs to a disease which is found very commonly among the seminomad villagers along the banks of the Euphrates River. It is usually contracted in childhood and manifests itself first as an eruption of

the skin and mucous membranes. This stage usually passes without apparent organic damage, but at some subsequent time inflammatory sequelae usually appear in the skin, the nasopharynx or the periosteum of the long bones.

With the use of the dark field, Hudson has been able to demonstrate spirochetes of the characteristic morphologic appearance and motility of Spirochaeta pallida in the lesions in fresh infections.

Protocols of typical cases of bejel are given. They show that this disease is highly contagious and is usually contracted by and from children; that it is an afebrile malady, with little effect on the general constitution; that it usually exhibits mucous and cutaneous lesions in the early stages, with occasional involvement of the periosteum; that it retains the activity and contagiousness of the early lesions up to one year or more; that it often becomes contagious again many years later in mucocutaneous relapses; that it is uniformly accompanied by positive precipitation and complement fixation reactions in the blood, and that it responds very favorably and very quickly to intramuscular bismuth therapy.

The apparent absence in bejel of an initial lesion of the type known as chancre in venereal syphilis is noteworthy.

GENGENBACH, Denver.

THE PSYCHOLOGY OF JUVENILE PARETIC NEUROSYPHILIS. W. C. MENNINGER, Psychoanalyt. Rev. **23**:76 (Jan.) 1936.

In a previous study based on 43 cases studied personally and 610 cases reported in the literature, Menninger recorded the observation that the mental picture most typical of juvenile dementia paralytica is progressive dementia. Delusions were present in 19 per cent of the patients, with 9.5 per cent expansive or grandiose and 4.3 per cent paranoid. Euphoria was present in 17.6 per cent of the patients, and depression, in only 8.6 per cent. Infantile personal habits and mannerisms were frequent; conspicuous manual masturbation was commonly reported; 43.3 per cent of the patients showed untidy excretory habits; dancing, bouncing in bed, collecting waste and trinkets, stroking the hair, pulling at the nose or ears and grimacing were much more common in juvenile than in adult dementia paralytica.

These figures are significant in indicating differences in mental picture in the juvenile and the adult type. They suggest the special points to be studied in the psychologic picture of the juvenile form, namely, the dementing process, the *petite* expansive delusions, the rarity of depression and the frequency of infantile mannerisms.

The dementia is due in part to destruction of the brain. In addition, there is evidence of the important mechanism of regression in the psychoanalytic sense, both of libido distribution (object-finding phases) and ego development. In psychosexual development the patient with juvenile dementia paralytica rarely reaches even the homo-erotic level, and in none of Menninger's cases did one reach adult heterosexual development. Often an effort toward homosexual adjustment is to be observed, but in nearly every case it is apparent as the disease progresses that interest (libido) is withdrawn from the external environment and exhibitionism, sadism, masochism and auto-eroticism in other forms become more common. This regression is suggested by the early symptoms of the disease—dulling and withdrawal of former interest in persons and objects, sensitiveness and timidity. The regression is progressive to levels of simpler functioning, and as the disease reaches the terminal stage, there are nearly complete withdrawal of interest (libido) investment from the external environment and entire fixation on the patient (absolute narcissism). In contrast to the adult type of dementia paralytica, in which progressive deterioration usually results in elaborate compensatory efforts, such as delusions of omnipotence and other psychotic symptoms, the juvenile type reaches a primitive, infantile, auto-erotic, tube-fed, vegetative state, suggesting intra-uterine life.

The majority of patients with juvenile dementia paralytica show simple deterioration rather than the psychotic reaction usual in the adult form, for two reasons: 1. The ego ideal is incompletely developed and weakly differentiated

at the age of onset of the illness in most cases of the juvenile type. 2. A stormy pathologic cerebral process may stir the psyche to a more aggressive compensatory activity than a slowly developing disease, which would result in deterioration rather than in mania or melancholia of the dementia paralytic type. This, indeed, must be the case in juvenile dementia paralytica.

Depression is infrequent and is rarely associated with self-depreciation and self-accusations, but there is loss of self-esteem, usually from thwarting or rebuff. Patients with juvenile dementia paralytica respond with a compensatory projection of their inadequacy. Likewise, the expansive delusions are poorly formed not because of immature development of the ego ideal alone. The child has not reached a point at which major conflicts may arise about potency or creativeness. The counterpart symptoms of euphoria and braggadocio are frequent, with a complacent attitude of well-being. It seems that this results through regression to a simpler level of life (ego development) at which prohibitions are fewer and the unconscious insight, previously perceived, may be ignored. Thus, it constitutes an overcoming of inadequacy and painful consciousness of the disease.

Probably the most important psychologic trauma experienced by the patient with juvenile dementia paralytica is the recognition of mental failure, evidence of which constitutes one of the earliest symptoms. The patient talks of his mental failure without real understanding of it. He reacts to the unconscious recognition of his loss first with depression and projection in mild ideas of reference, and occasionally in paranoid delusions; he then regresses to an earlier psychologic stage of development, at which the inadequacies can be glossed over and compensated for by euphoria and delusions of childish power and satisfaction.

KARPMAN, Washington, D. C. [ARCH. NEUROL. & PSYCHIAT.]

SOURCES OF INFECTION IN PRIMARY TUBERCULOSIS OF CHILDHOOD. C. H. C. TOUSSAINT and E. J. MACINTYRE, Brit. J. Tuberc. **30**:125 (July) 1936.

An effort was made to trace to its source the infection responsible for the deaths of eighty children aged up to 10 years, most of whom succumbed to miliary tuberculosis or tuberculous meningitis. The contacts of twenty-six of the children refused to be examined. Of the remaining fifty-four children 46 (85.2 per cent) were found to have a probable source of their infection in a human being—the father in twenty-six cases, the mother in seven, both parents in one and other persons in twelve. In three other cases, a human source was possible. In five cases no human source of infection was found. While human sources of infection were responsible for most of the deaths in the series, the authors admit that in the British Isles other investigations have shown that in 25 per cent of cases tuberculous meningitis is due to bovine infection. For the prevention of tuberculous infection in infancy through human contacts three main lines of procedure are suggested: immunization of children exposed to risk with BCG; boarding out of contacts; segregation of persons whose sputum shows the bacilli.

EUGENE SMITH, Ogden, Utah.

CONGENITAL ABSENCE OF A PART OF THE OCCIPUT DUE TO CONGENITAL SYPHILIS. J. NICOLAS and J. ROUSSET, Bull. Soc. franç. de dermat. et syph. **43**:5, 1936.

An 18 year old girl entered the hospital for treatment of urethritis. On examination it was discovered that a part of the osseous portion of the occiput was missing. Palpation revealed a depression which corresponded to a point which in roentgenograms of the skull showed complete absence of bone. The deformity measured 7 by 5 cm. and was covered by apparently normal scalp. Schüller-Christian disease was ruled out, and although the Wassermann and Kahn tests were negative the authors felt that the process was most probably of syphilitic origin, especially as a diagnosis of syphilis had been made in the case of the patient's mother several years previously.

LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

DEATH OF A NEW-BORN INFANT FOLLOWING INGESTION OF BCG. GUÉRIN-VALMALE, VERDEUIL and DOR, Bull. Soc. d'obst. et de gynéc. **25**:389 (May) 1936.

A boy weighed 2,950 Gm. at birth. During the first three days he lost 150 Gm., but within the next two days he gained 40 Gm. and seemed well. He was then given a dose of BCG apparently orally. The mother had requested that the measure be taken because two of her brothers had died of meningitis, presumably tuberculous. From then on the infant lost weight progressively and died at the age of 22 days, weighing 600 Gm. less than at birth. All therapeutic measures, including change of diet, failed to check the downward course. Breast milk was given at first, though there seemed to be no disgestive disturbance. The temperature had been normal except for a rise to 39 C. (102.2 F.) on the day the vaccine was given and again eight days later. Gross and microscopic examination of the viscera showed no abnormality. The mesentery, however, was studded with slightly injected lymph nodes varying in size from that of a small granule to that of an apple seed. The microscopic appearance of the nodes is described. It was not typical of tuberculosis, and bacilli could not be demonstrated in smears of the tissue. From the appearance of the glands, however, the authors believe that death was caused by some acute infection of gastro-intestinal origin. They state that ingestion of BCG often temporarily reduces the resistance of infants and renders them susceptible to intercurrent infections. Several other deaths in infants have been reported to have followed the ingestion of BCG. It is considered that the administration of BCG is not without danger and should not be practiced as a routine.

GLASER, Rochester, N. Y.

TREATMENT OF CONGENITAL SYPHILIS. E. LESNÉ and A. LINOSSIER-ARDOIN, Nourrisson **24**:197 (July) 1936.

Best results in the treatment of congenital syphilis have been obtained with the trivalent arsenical compounds, especially neoarsphenamine and sulfarsphenamine. Only in cases of overwhelming syphilitic infection is it thought advisable to give a preliminary course of bismuth therapy before resorting to the treatment with arsenic. The various reactions and contraindications for the use of arsenical compounds are cited in detail. It is claimed that unfavorable reactions are encountered much less frequently in infants than in adults. For interstitial keratitis best results are obtained by first giving a course of injections with mercuric cyanide; these are followed by treatment with one of the arsphenamines.

MCCLELLAND, Cleveland.

SPASMODIC PARAPLEGIA WITH CEREBRAL DISTURBANCE IN CONGENITAL SYPHILIS. A. B. MARFAN, Rev. franç. de pédiat. **12**:1, 1936.

Spasmodic paraplegia occurs most frequently between the ages of 4 and 12 years. The spastic paralysis is noticed particularly when there is an attempt to walk and is not manifest when the child lies quietly in bed. It is not associated with disturbance of sphincters or of sensibility but may be associated with psychic disturbances, such as emotional imbalance. The pupils of the eye show the Argyll Robertson sign, and frequently there is also interstitial keratitis. The Wassermann reaction of the blood and that of the spinal fluid are positive. Treatment may be of some help in retarding the progress of the condition but usually does not cure it.

LESLIE, Evanston, Ill.

SUBACUTE CONGENITAL SYPHILITIC MENINGITIS RESEMBLING TUBERCULOUS MENINGITIS. ROBERT DEBRÉ, JULIEN MARIE and A. BERNARD-PICHON, Rev. franç. de pédiat. **12**:17, 1936.

In eight cases occurring among infants and children the clinical symptoms closely resembled those of tuberculous meningitis. Negative tuberculin tests and failure to find tubercle bacilli in the spinal fluids rendered this diagnosis

improbable. Positive Wassermann reactions in blood and spinal fluid and histories of syphilis in the parents or positive serologic reactions in one or both parents established the diagnosis of syphilitic meningitis. The prognosis is better in older children than it is in young infants, in whom it is more likely to be a manifestation of a rather overwhelming infection. LESLIE, Evanston, Ill.

STATISTICAL STUDY OF CUTANEOUS TUBERCULIN REACTIONS IN CHILDREN AGED BETWEEN TWO AND SEVENTEEN YEARS IN THE PARISIAN AREA. M. COFFIN, Rev. franç. de pédiat. **12**:486, 1936.

Coffin has studied the distribution of positive and negative tuberculin reactions in a group of 343 children between the ages of 3 and 17 years, living in Paris. The results are given according to age. In all there were only 113 positive reactions. This indicates a definite decrease in the course of twenty years.

LESLIE, Evanston, Ill.

CLINICAL AND STATISTICAL STUDY OF THE MORBIDITY AND MORTALITY OF FIVE HUNDRED CHILDREN OF TUBERCULOUS MOTHERS. A. GUERRA and G. SANNA, Lattante **7**:531 (Nov.) 1936.

During the years 1930 to 1934 five hundred infants of tuberculous mothers have from the first few days of life been under the supervision of the Provincial Institute for Protection and Assistance of the Infants of Milan. Fifty-eight per cent of the infants were illegitimate.

The weight of the children at birth tended to be lower than normal, as many as 14 per cent showing congenital debility. Thirty-eight per cent showed an abnormally slow gain in weight in the first month of life. Ninety-four infants died, the majority (65) in the first six months of life, 52 of respiratory infections, 11 of gastro-intestinal disturbances, and 16 of prematurity; congenital debility was a definite contributory factor in many of these deaths. Only four died of tuberculous infection.

The morbidity and mortality among 100 foundlings was very similar to that of the group with tuberculous mothers.

Of 486 tuberculin tests made on the children at various ages and times, only 8 were positive. HIGGINS, Boston.

HEMATOGENOUS TUBERCULOSIS IN INFANCY. E. JASO ROLDÁN, An. de pediat. **2**:75 (Feb.) 1935.

The author gives a summation of the findings produced by autogenous tuberculosis in the various organs and body structures. HERRON, Spokane, Wash.

INFLUENCE OF HEREDITY AND ENVIRONMENT ON THE SIZE OF THE HEART: INVESTIGATIONS BASED ON TWINS. J. B. GUREWITSCH, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:62 (July) 1936.

In 107 pairs of identical and 86 pairs of nonidentical twins the size of the heart was studied orthodiagraphically. The influence of hereditary and environmental factors was estimated statistically. Paratypical factors were found to play the most important rôle in determining the size of the heart. Infections in the remote past (one to one and one-half years before) appeared to be of minor importance in this respect. The paper supplies useful bibliographic material.

MCCUNE, New York.

THE COURSE OF THE AORTA IN CHILDREN AND ITS MENSURABILITY. S. KREUZFUCHS, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:396 (Oct.) 1936.

Measuring the diameter of the aorta of a child presents peculiar difficulties, which are related to the shape of the thorax and the course of the superior portion

of the aorta. The measurement of the ascending portion of the aorta is approximately as unreliable as in adults. The author describes a technic by which some of these dimensions may be measured and discusses the results of such studies. Additional investigations are in progress.

McCUNE, New York.

PULMONARY TUBERCULOSIS IN CHILDHOOD. ASPARUCH PANOFF, Monatschr. f. Kinderh. **66**:107 (July) 1936.

Panoff gives a series of case reports including temperature curves and roentgenograms, which were of interest to him. His studies lead to the suggestion that fever may be a prodromal stage of tuberculosis and may be present before any objective findings. In several cases persons giving negative reactions to tuberculin gave positive reactions after several weeks of fever. He reports cases of epituberculosis and also of chronic miliary tuberculosis without fever. His statistics comparing the frequency of positive reactions to tuberculin in the urban and rural populations of Bulgaria are significant. At 16 years of age, 73 per cent of the population of Sofia showed positive Pirquet reactions, while in the country only 27 per cent of the children reacted positively.

GERSTLEY, Chicago.

ACTIVATION OF THE SPECIFIC TREATMENT OF SYPHILIS BY THE SUBCUTANEOUS INSUFFLATION OF OXYGEN: A PRELIMINARY COMMUNICATION. M. A. ROSENTUL, A. D. BOGODAROV, M. M. PLOTKINA and A. M. KHALETZKAYA, Vrach. delo **19**:1037, 1936.

Subcutaneous introduction of oxygen is known to have a marked influence on the vital processes, leading to increase in their activity as well as to neutralization and quicker elimination of the toxic products of metabolism. On the basis of these observations, Professor Rosentul introduced subcutaneous insufflation of oxygen as an auxiliary method for the treatment of syphilis. Experimentally it was revealed that subcutaneous introduction of oxygen makes rabbits more tolerant to the action of neoarsphenamine, an observation which the authors believe is due to an increase in the oxidative processes of the body, which in its turn leads to more rapid and complete oxidation of neoarsphenamine and its products.

The combined neoarsphenamine-bismuth-oxygen treatment was used in 140 patients suffering from recent syphilitic infection. The patients were given from twenty to twenty-five insufflations of oxygen (doses of from 300 to 400 cc.) forty or sixty minutes before or after the introduction of the drug, an insufflation being made on the average every second day. The time necessary for the complete disappearance of the spirochetes from the lesions was compared with that necessary in the controls. The favorable therapeutic results obtained led the authors to conclude that this is the method of choice in the treatment of early syphilis, particularly if the patients are debilitated or if they do not tolerate well neoarsphenamine alone.

BODER, Los Angeles

Diseases of Blood, Heart and Blood Vessels and Spleen

A METHOD FOR DETERMINING THE SEDIMENTATION RATE AND RED CELL VOLUME IN INFANTS AND CHILDREN WITH THE USE OF CAPILLARY BLOOD. CARL H. SMITH, Am. J. M. Sc. **192**:73 (July) 1936.

A method and technic for the determination of the sedimentation rate and red cell volume is presented, a reduced macrosedimentation tube embodying the basic requirements of apparatus in which sedimentation tests are carried out with venous blood. Close agreement was noted in 102 determinations with this method in addition to 128 other microsedimentation tests and with a standard test utilizing venous blood. The average rates of settling in normal infants and children was

4.2 mm. for one-half hour and 9.1 mm. for 1 hour, a 5 per cent solution of sodium citrate being used as an anticoagulant. The range of cell volume in this group was 30 to 40 per cent (average, 35.8 per cent). It is suggested that whenever possible the cell volume percentage be reported together with the sedimentation rate. The rate of settling may then be evaluated in accordance with the extent to which the cell volume percentage approximates the range of normal instead of substituting for it a value derived by comparison with an arbitrary standard.

HENSKE, Omaha.

BLOOD STUDIES IN INFANCY: A COMPARISON OF THE RED CELL COUNTS AND HEMOGLOBIN VALUES OF PREMATURE INFANTS AND TWINS WITH THOSE OF FULL-TERM CHILDREN. ALICE STEWART, Brit. J. Child. Dis. **33**:165 (July-Sept.) 1936.

This study was conducted at the Manchester Babies' Hospital and was confined to cases of prematurity, malnutrition and chronic dyspepsia. The majority of observations were made on infants in the first twenty-eight weeks of life. Altogether, sixty-one infants were studied.

A rapid reduction in hemoglobin content was found immediately after birth, the maximum drop occurring between the ninth and the eleventh week.

The number of red cells also fell, but the color index remained high and was often greater than 1.

After the third month there was a gradual rise in hemoglobin content and red cell count until the sixth month. In full term children the hemoglobin content reached a higher level than in twins or premature children, but the average counts showed little difference in the two series.

It was rare for the color index to be low before the seventh month. The average at this age was 0.92.

LANGMANN, New York.

INTRAVENOUS INJECTION OF HYPERTONIC SODIUM CHLORIDE SOLUTION IN THE TREATMENT OF SOME CONDITIONS OF LOW BLOOD-PRESSURE. JOAN B. WALKER, Brit. J. Surg. **24**:105 (July) 1936.

Walker elucidates the conditions produced by a spinal anesthetic. A lowering of the blood pressure most frequently occurs. As spinal anesthesia is the method of choice in intestinal obstruction, various measures were investigated to alleviate or prevent the occurrence of hypotension.

It was found that the type of shock present in spinal anesthesia is similar to experimental traumatic shock in animals, in which the blood stagnates in the injured limbs; in spinal anesthesia there is stagnation of the blood in the anesthetized and paralyzed regions. The most effective treatment consisted of giving about 40 cc. of a 30 per cent solution of sodium chloride intravenously. This resulted in an immediate stimulation of the circulation and an increase of blood pressure within five minutes after the injection. After from twenty to thirty minutes, when the body fluids had become readjusted, the blood pressure readings were on a lower level but not on the level characteristic of a state of shock.

SUMMERFELDT, Toronto, Canada.

TECHNIQUE OF SPLEEN PUNCTURE. L. E. NAPIER, Lancet **2**:126 (July 18) 1936.

In the course of fifteen years Napier, who is in charge of the kala-azar inquiry in the School of Tropical Medicine in Calcutta, India, has performed over 5,000 splenic punctures. He does not regard it as a dangerous procedure. The special syringe which he uses and which is fully described in the article can be operated with one hand, the other being free to locate and to fix the spleen. The value of splenic puncture as a diagnostic procedure in conditions other than kala-azar has not yet been fully explored.

LANGMANN, New York.

FEBRILE ANAEMIA OF OBSCURE ORIGIN. F. D. HART, Proc. Roy. Soc. Med. **30**:403 (Oct.) 1936.

A case is reported in a boy of 5 years. Eight months before admission to the hospital he was treated by mastoidectomy and made a normal recovery but did not gain following that. About one month previous to admission he commenced to cough, have a fever and complain of headache. The blood at admission showed 1,500,000 red cells per cubic millimeter, with hemoglobin, 25 per cent, and 3,000 white cells. A differential count showed polymorphonuclears 8 per cent, lymphocytes 91 per cent and monocytes 1 per cent. Four normoblasts were seen among 200 white cells counted. Marked anisocytosis and polychromasia were present. The spleen was not enlarged. A transfusion of 300 cc. of the father's blood was given. Daily blood counts are given in the report, and a postscript, made two and a half months later, stated that the red cell count was 3,300,000, with hemoglobin 55 per cent, but the spleen and liver were greatly enlarged. The inguinal, axillary, lacrimal, jugular and submaxillary glands were swollen. The left parotid gland was much enlarged and was discharging pus. The condition at that time was thought to be lymphatic leukemia.

WILLIAMSON, New Orleans.

SECONDARY OR SYMPTOMATIC ERYTHROBLASTOSIS. N. J. SPYROPOULOS, Rev. franç. de pédiat. **12**:504, 1936.

Spyropoulos reports two cases of malaria, three cases of leishmaniasis, two cases of chronic purulent tonsillitis, two cases of infectious jaundice, one case of dietary anemia and two cases of anemia of eaters of dirt in which the appearance of the normoblasts in the blood smear was a striking feature. There were also marked anisocytosis and poikylocytosis, as well as splenic enlargement, in all the cases. With recovery the normoblasts disappeared from the blood. The author states that the appearance of normoblasts in similar conditions is rare, and he thinks that this response may be due in part to a constitutional peculiarity or in part to the young age of most of these patients.

LESLIE, Evanston, Ill.

SPLENECTOMY IN A CASE OF ERYTHROBLASTIC ANEMIA (COOLEY). R. S. CUIZZA, Clin. pediat. **18**:671 (Nov.) 1936.

Twenty months after splenectomy was performed on a 3 year old child because of typical Cooley's anemia, the child showed great improvement without apparent change in the underlying process. Cuizza recommends splenectomy for patients with this condition.

DOOLEY, New York.

THE HEMO-OSTEOPATHY OF COOLEY. M. ORTOLANI and G. CASTAGNARI, Lattante **7**:549 (Nov.) 1936.

Case reports of seven cases of Cooley's anemia are used as the basis of a discussion of this syndrome, for which the authors prefer the name hemo-osteopathy of Cooley. Two of the patients were identical twins. Excellent photographs and x-ray prints are shown.

HIGGINS, Boston.

PATHOLOGIC GRANULES IN LEUKOCYTES IN CHILDREN. VICTOR KOSZLER, Arch. f. Kinderh. **106**:163, 1935.

The presence of pathologic granules in polymorphonuclear leukocytes is found in a higher percentage of well childlren than reported by Mommsen. In children affected by serum sickness and vaccination the findings were similar to those of Mommsen in patients with infectious diseases. The maximum appearance of pathologic granules coincides with the high point of the illness.

CRANE, Washington, D. C.

COMPARATIVE STUDIES OF THE THROMBOCYTE VALUES IN CHILDHOOD. P. KASSAY-FARKAS, Arch. f. Kinderh. **109**:29, 1936.

Comparative studies of the thrombocytes in 200 children according to the methods described by Jürgens and Fonio showed the following results:

For 70 per cent of the children the values were lower by Fonio's than by Jürgens' method, for 12 per cent approximately the same and for 18 per cent higher. No constant relationship was demonstrated between the age of the child and the thrombocyte value (Jürgens' method). According to Jürgens' method, the thrombocyte values remain constant; according to the method of Fonio, marked variations appear. There is no constant relationship between blood group and height of the thrombocyte values.

CRANE, Washington, D. C.

VEGETATIVE REGULATION OF THE RED BLOOD CELLS. H. KINKEL and G. DIERCKS, Monatschr. f. Kinderh. **67**:229 (Nov.) 1936.

With the idea that the sympathetic and parasympathetic systems regulate the discharge of red cells from bone marrow as though by the opening and closing of a door, the writers tried the effects of various drugs on the blood picture. Pilocarpine and acetylcholine were used as parasympathetic stimulants and atropine as a parasympathetic depressant. Epinephrine, racemic ephedrine and ephedrine were used as sympathetic stimulants and ergotamine as a sympathetic depressant. Results were somewhat inconclusive, because the course of the various nerve fibers has not been accurately traced through the bone tissues and also because the taking of food has an effect which must be taken into consideration.

GERSTLEY, Chicago.

PARALYSIS ASSOCIATED WITH HEMOPHILIA. H. GÜNTHER, Monatschr. f. Psychiat. u. Neurol. **91**:33 (April) 1935.

In patients with hemophilia meningeal hematoma is observed with considerable frequency, but hemorrhages into the substance of the brain or spinal cord have not been conclusively demonstrated. Hematomas of the extremities may damage near-by peripheral nerves. Effusion of blood into the iliopsoas muscle, with involvement of the femoral nerve, is relatively common. This muscle must be especially susceptible to hemmorhage, since it is well protected from direct injury. The nerve is damaged by pressure of the extravasated blood, which may diffusely infiltrate the whole muscle. Three cases illustrating this type of involvement are reported briefly. In addition to local pain and swelling, there was paralysis or paresis of the quadriceps extensor femoris muscle, with absence of the patellar reflex and sensory impairment in the area of skin supplied by the femoral nerve.

ROTHSCHILD, Foxborough, Mass. [ARCH. NEUROL. & PSYCHIAT.]

CEREBRAL HEMORRHAGE COMPLICATING WERLHOF'S DISEASE. E. TRAUB, Ztschr. f. Kinderh. **58**:67 (May 20) 1936.

Cerebral hemorrhage complicates Werlhof's disease relatively rarely. Although a number of cases have been reported in pediatric literature, only two can be regarded as having been proved to be cases of essential thrombocytopenia. Traub reports a case which terminated fatally. Although thrombocytopenia was extreme (despite numerous megakaryocytes in the bone marrow), he is of the opinion that damaged capillary endothelium is of greater importance in the etiology of hemorrhagic manifestations. Hematuria is regarded as being of especial prognostic significance.

SIEMSEN, Chicago.

CORRELATION BETWEEN BLOOD PRESSURE AND HORMONAL SECRETION IN CHILDREN. G. SURÁNYI and K. FEJES, Orvosi hetil. **80**:996 (Oct. 17) 1936.

The examinations were made with the tonoscillograph of Plesch. The blood pressure in diabetic children was diminished. These children showed a sudden

rise of blood pressure and tachycardia after subcutaneous injection of 0.2 cm. of epinephrine. It may be that diabetic children react to the injection of epinephrine so suddenly because their constant hypotonia is caused by a diminution in the production of this substance. Such an injection is not always followed by a rise in blood pressure and tachycardia, because in the smaller part of the examined cases those children who from all points of view seemed to be healthy did not show the usual symptoms but a slighter lowering of the blood pressure and bradycardia.

GÖTTCHE, Budapest, Hungary.

CEREBRAL REGULATION OF THE BLOOD SUGAR LEVEL IN CHILDHOOD. P. ROBOZ and E. RAUSNITZ, Orvosi hetil. **80**:1139 (Nov. 28) 1936.

The level of the blood sugar of children from 7 to 14 years old showed no notable changes after doses of aminopyrine (15 mg. per kilogram of body weight). In other children a decided lowering or raising of the level occurs. This vacillation was observed in the blood sugar of children who showed many disorders of the vegetative nervous system. The method seems to be good for the examination of the blood sugar center. When the vacillation of the blood sugar level is greater than ± 10 to 15 per cent, the center is in a vacillating condition.

GÖTTCHE, Budapest, Hungary.

TREATMENT OF PAROXYSMAL TACHYCARDIA WITH ACETYLCHOLINE. P. KISS, Orvosi hetil. **80**:1188 (Dec. 12) 1936.

An attack of paroxysmal tachycardia which had lasted twenty hours ended twenty-six minutes after an intramuscular injection of acetylcholine.

GÖTTCHE, Budapest, Hungary.

A STUDY ON THE GASES IN THE UMBILICAL BLOOD. M. NOGUCHI, Jap. J. Obst. & Gynec. **19**:328 (July) 1936.

Investigation of the oxygen and carbon dioxide contents of the blood in the umbilical artery and vein of normal and of asphyxiated infants shows a decrease of both gases in the blood of asphyxiated infants. This is slight in the case of carbon dioxide and marked in the case of oxygen. Meconium frequently occurs in the amniotic fluid in infants with a normal amount of oxygen in the fetal blood.

ADAIR and POTTER, Chicago.

THROMBOPENIA IN CHILDHOOD. W. K. DICKE, Nederl. tijdschr. v. geneesk. **79**:5748 (Dec. 14) 1935.

A record is made of two cases of Werlhof's syndrome in children, one in a girl of 3 years, occurring symptomatically and issuing in spontaneous recovery, the other in a boy of 12 years, idiopathic with recovery after splenectomy. Whether these recoveries are to be considered definitive cannot be said at present, after one and a half years, as recurrences may occur even up to ten years.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

A COMPARISON OF INTRADERMAL AND INTRAMUCOSAL TESTS IN CASES OF ALLERGIC RHINITIS. LLOYD D. LINTON, Arch. Otolaryng. **23**:679 (June) 1936.

After comparing the results obtained by intradermal tests with those secured by intramucosal tests in cases of allergic rhinitis, Linton states that the former are not a reliable index of the mucosal sensitivity. Of seven patients showing aural symptoms, six had these identical symptoms induced by intramucosal injection of allergen into the nose. Likewise, identical symptoms were caused in

allergic patients giving a history of headache, asthma and ocular pain. He concludes that even though the patients have reacted negatively to cutaneous tests, the allergens to which they are sensitive can be determined by intramucosal tests.

GREENWOOD, Chicago.

EFFECTS OF BACTERIAL TOXINS IN THE MIDDLE EAR. ELLISON L. ROSS and R. W. RAWSON, Arch. Otolaryng. **24**:51 (July) 1936.

Observations of the effects of numerous bacterial toxins placed in the middle ear were made by Ross and Rawson. The vestibular and auditory functions were noted. Experimental work was done on dogs and included the injection of the toxins of hemolytic streptococci, pneumococci and Staphylococcus aureus and those of the organisms of tetanus, scarlet fever and diphtheria. Injections of the first four resulted in no significant vestibular or auditory changes, whereas the toxin of scarlet fever produced slight reactions in three of four animals. However, the diphtheria toxin resulted in the destruction of both the vestibular and the auditory processes. Reports found in the literature are reviewed, and the conclusion is drawn that the middle ear may carry any toxin in it into the endings of the eighth nerve.

GREENWOOD, Chicago.

AVERAGE RANGE OF ACUITY OF HEARING OF HIGH SCHOOL PUPILS. IRENE B. YOUNG, Arch. Otolaryng. **24**:76 (July) 1936.

A study of the hearing of pupils at Horace Mann High School of Teachers College, Columbia University, was conducted over five years. The average age range was determined. The methods, conditions and technic of testing are given. In all probability the obtained mean was above the expected norm calculated from other data because of more favorable testing conditions and the high intelligence quotients of the persons tested.

GREENWOOD, Chicago.

ALLERGY AS RELATED TO OTOLARYNGOLOGY. C. C. SWANN, Arch. Pediat. **53**:730 (NOV.) 1936.

In from 20 to 30 per cent of cases sinus disease is allergic in origin, and in cases in which the disease is chronic the incidence of allergy is much greater. Any patient with a history of frequent colds, sneezing, itching of the nasal mucous membranes, nasal discharge and nasal obstruction, with edema and pallor of the mucous membranes, should receive a thorough study to determine the possibility of sensitivity to protein.

ORR, Buffalo.

A COMPARATIVE STUDY OF HEMOLYTIC STREPTOCOCCI ISOLATED FROM THE THROATS OF RESIDENTS OF NEW ORLEANS AND NEW YORK. P. TEIGER and B. C. SEEGAL, J. Bact. **32**:631 (Dec.) 1936.

The authors state that a study of the geographic distribution of rheumatic fever, scarlet fever and acute glomerulonephritis in Canada and the United States has shown that two of these three diseases, rheumatic fever and scarlet fever, diminish in frequency in the South, while acute nephritis remains approximately as frequent in the South as in the North. Since clinical and laboratory data indicate that acute glomerulonephritis is usually initiated by an infection with hemolytic streptococci, it appeared peculiar that the incidence of this disease failed to diminish in the southern part of the United States while the incidence of the other two diseases due to hemolytic streptococci did decrease.

A series of throat cultures was obtained from patients with acute nephritis and acute pharyngitis and from normal persons (controls) living in New Orleans, and 63 strains of hemolytic streptococci were isolated. These were brought back to New York and compared with 103 strains isolated in throat cultures taken in New York City. The organisms were examined for their fermentation of lactose, mannitol and salicin, their hemolysis in blood pour plates, their production of a

soluble hemolysin and skin toxin, their hydrolysis of sodium hippurate and their final p_H in dextrose broth. In these tests no difference was found between the hemolytic streptococci isolated from the throats of residents in New Orleans and New York.

STOESSER, Minneapolis.

TOTAL AND PERMANENT DEAFNESS FROM PAROTITIS. J. H. BRISTOW, J. Michigan M. Soc. **35**:175 (March) 1936.

A 9 year old girl had a bilateral parotitis, followed by progressive nerve deafness resulting in permanent total deafness.

CAREY, Detroit.

RETROPHARYNGEAL ABSCESS. L. RICHARDS, New England J. Med. **215**:1120 (Dec. 10) 1936.

Richards reports a series of 162 cases of retropharyngeal abscess seen at the Children's Hospital in Boston during the past ten years. The fatalities numbered 12, or 7.4 per cent. The oldest patient was 12 years of age; the youngest, 4 months. By far the greatest number of patients were between the ages of 6 months and 3 years. Previous illnesses included sore throat in 22, otitis media in 21, cervical adenitis in 46 (glands previously incised in 8), head colds in 26, tuberculosis in 2, unexplained fever in 16, measles in 3 and nephritis in 1. The chief complaints included dyspnea (noisy breathing, snoring, cyanosis) in 61, dysphagia (regurgitation, anorexia, refusal) in 59, swollen neck in 37, stiff neck in 31, sore throat in 9, fever in 27, cough in 3 and convulsions in 2.

The present illness merged with the previous history, but, on an average, the symptoms due to the retropharyngeal abscess were of about four days' duration. Inspection and palpation of the throat were the two major methods of examination, yet both palpation and inspection have resulted disastrously in more than one able operator's experience. Except in cases of dire urgency, use should be made of a lateral roentgenogram of the neck.

The treatment for retropharyngeal abscess is drainage, which is accomplished by an incision made internally through the posterior pharyngeal wall or externally through the soft tissues of the neck. The operative procedures in this series of patients included incision (pharyngeal) in 135, external incision in 2, previous incision in 5 and transtonsillar incision in 2. In 18 cases some form of general anesthetic was administered, 14 patients receiving ether and 4 gas and oxygen. In the other 144 cases no anesthetic was administered. Four patients were operated on in the upright posture. The remainder, as far as direct mention was made of the position, were operated on in the prone or exaggerated prone, so-called Rose, position.

In 115 cases the outcome was recorded as uneventful. In 4 instances tracheotomy was necessary; in 8 there was prolonged sepsis; in 14 supplementary or secondary incision into the abscess cavity was deemed advisable; in 8 secondary incision of infected cervical glands was necessary; in 12 incision was followed by a fever in which for some reason or other the temperature failed to return to normal; in 3 there was severe hemorrhage, and finally in 17 there were so-called late complications, such as meningismus, pneumonitis, otitis media, sinusitis, scarlet fever or unexplained cough.

Sudden, severe, profuse hemorrhage, often recurrent, has been one of the most dreaded complications of retropharyngeal abscess. There were 3 instances in which such hemorrhage occurred, in 2 of which it proved fatal. Sudden severe hemorrhage must at once be controlled by ligation of the carotid artery.

GENGENBACH, Denver.

IMPORTANCE OF MIDDLE EAR INFLAMMATION AND MASTOIDITIS IN INFANCY FROM THE PEDIATRIC STANDPOINT. J. CSAPÓ, Arch. f. Kinderh. **109**:203, 1936.

Inflammation of the middle ear and the connected parts can produce a variety of clinical symptoms in infancy. The following forms are distinguished: the meningeal form; otogenic sepsis; septic, toxic and septicotoxic middle ear inflam-

mation, antral empyema or mastoiditis. Middle ear infection is one of the most important complications of dysentery in infancy and early childhood. Correctly timed paracentesis or trepanation will aid greatly in relieving the intestinal symptoms in such cases.

CRANE, Washington, D. C.

DEVELOPMENT OF THE ACCESSORY NASAL SINUSES. H. RICHTER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **141**:54, 1936.

Richter directs attention to a report about the normal development of the human nose, particularly of the ethmoid bone, which he published in 1932. He arrived at the conclusion that in the temporal bone, as well as in the accessory nasal sinuses, the stimulus for the pneumatization goes out from the mucous membrane. He speaks of a pneumatizing power of the mucous membrane and points out that he himself and M. Schwarz demonstrated the fundamental significance of the pneumatizing power of the nasal mucous membrane for the development of the accessory nasal sinuses. Sitsen, who studied the structure and the development of the frontal sinus, however, arrived at the conclusions that the mucous membrane does not take part in the pneumatization.

Because Sitsen failed to mention Richter's studies, and since Richter gave particular attention to the processes in the mucous membrane and to those of the adjoining bones, i. e., to the process of pneumatization, he decided to analyze Sitsen's report. He emphasizes that the accessory nasal sinuses appear in the fetus at different times. The maxillary sinus and the first traces of the ethmoid cells (cribral pockets) and of the sphenoid sinus appear first. The later frontal sinus is one of those cribral pockets which develop as protrusions of the median nasal duct. Since the frontal sinus is originally a cribral pocket, its origin and development are essentially the same as those of the other cribral pockets and accessory sinuses. Richter chose the ethmoid sinus for his studies for dimensional reasons, but he says that there is no reason to assume that the frontal sinus has a different origin. In his earlier report he demonstrated that the ethmoid cells develop by active ingrowth of nasal epithelium into the embryonal connective tissue. The presence of the cartilaginous nasal capsule does not prevent further development of the hollow spaces. On the contrary, resorption of the cartilage takes place. The basin-like resorption of the cartilage results in long cartilaginous protrusions, which become septums of some of the ethmoid cells. Ossification sets in later. Richter emphasizes that all these processes take place before birth, i. e., at a time when air pressure is out of the question. He regards the growth of the ethmoid sinuses during childhood as a result of new formation of bone on the outer surface of the bony cellular wall and of resorption of bone on the inner surface. This process begins during the seventh fetal month. He states further that it can be demonstrated that the frontal sinus is derived from the ethmoid bone. He admits that for the period after birth he cannot definitely deny the influence of external air pressure on the growth of the accessory nasal sinuses, but he feels that neither can such an influence be definitely demonstrated. However, he insists that there is definite proof that the development of the accessory nasal sinuses is the result of formative power in the mucous membrane.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

SOUND FEELING IN DEAF-MUTES AND ITS PRACTICAL SIGNIFICANCE. B. SCHINDLER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **39**:431, 1936.

Schindler directs attention to the fact that in the determination and estimation of extremely small remnants of hearing, hearing and feeling are easily confused. He reproduces a curve that indicates thresholds of feeling in the ears of deaf persons and a curve that indicates thresholds of tickling and pain in the ears of persons with normal hearing and of deaf persons. Further, he suggests methods which will enable every examiner to determine with his apparatus the intensity of feeling in deaf persons, which is extremely important for the differentiation of hearing and feeling.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

RESISTANCE OF CHILDREN TO REPEATED NOSOCOMIAL INFECTIONS OF THE UPPER RESPIRATORY TRACT. C. GYLLENSWÄRD, Acta pædiat. **19**:153, 1936.

In a children's home in Stockholm systemic records were kept of the incidence of nosocomial respiratory infections in children between 1 and 7 years of age; the observations extended over a five year period and embraced 638 children, who spent a total of 59,771 days in the institution. The results were examined statistically from the following points of view: age, sex, sensitivity to tuberculin, length of stay in the home, number of nosocomial infections, types of infection, percentage incidence of infection, time of onset of infection, duration of illness and complications. The infections were divided into two classes on the basis of severity, namely, those which were accompanied by an elevation of temperature as high as 37.5 C. (1,114 cases) and those in which the temperature rose to 38 C. (872 cases).

The first wave of respiratory infection affected children who were previously healthy on either the third or the tenth day after admission; the third day infections were mild; those of the tenth day, severe. After an interval of time another wave occurred. The infections which occurred during the fifth week after admission were relatively mild, while those which occurred during the sixth week were somewhat more severe. A third wave usually appeared six weeks after the second, and the infections showed different degrees of severity. In the fourth wave, those infections which appeared six weeks after the preceding one were severe, while those which appeared at seven weeks were milder. If the children remained in the hospital long enough, further outbreaks of infection occurred at similar intervals; however, the frequency of severe infections declined as did the number of children affected, and the duration of illness tended to become shorter. These observations suggest that recurrent respiratory infections enhance the immunity of those who suffer from them; this conclusion is strengthened by the fact that the younger children were infected more frequently than the older ones and that their illnesses were more severe. No difference was observed between the children of different sexes.

McCUNE, New York.

Diseases of Lungs, Pleura and Mediastinum

SPONTANEOUS TENSION PNEUMOTHORAX. H. W. ELGHAMMER, Arch. Pediat. **53**:490 (July) 1936.

Elghammer reports the occurrence of tension pneumothorax in a 4 year old girl, producing extreme displacement of the upper lobe of the left lung into the right thoracic cavity. The intrapleural pressure registered 48 mm. of mercury. A total of twenty-one aspirations to relieve the intrapleural pressure resulted in a disappearance of the pneumothorax. The author considers repeated aspiration a safer procedure than permanent open drainage.

ORR, Buffalo.

REACTIONS TO INTRACUTANEOUS INJECTIONS OF NUCLEOPROTEINS OF THE UPPER RESPIRATORY PATHOGENIC BACTERIA IN ASTHMATIC PATIENTS. FRANKLIN A. STEVENS and LEOPOLD JORDANI, J. Allergy **7**:443 (July) 1936.

Stevens and Jordani base their conclusions on the findings concerning 100 asthmatic patients, 31 of whom were sensitive to the common allergens and 69 of whom were not sensitive.

"1. Immediate and delayed reactions occur when bacterial nucleoproteins are injected intracutaneously in asthmatic persons.

"2. Both immediate and delayed reactions at the site of the same inoculation are infrequent.

"3. The reactions to the nucleoproteins are constantly changing. During a period of a few weeks positive reactions may disappear and reactions to other upper respiratory bacteria make their appearance.

"4. The immediate and delayed reactions are proportionately distributed among patients sensitive and nonsensitive to the common allergens."

HOYER, Cincinnati.

BLOOD SUGAR STUDIES IN HAY FEVER AND ASTHMA. E. L. MACQUIDDY, A. R. McINTYRE and DON DOSER, J. Allergy **7**:471 (July) 1936.

There is no significant difference between normal and allergic persons in regard to fasting blood sugar levels and response to the ingestion of 100 Gm. of dextrose. Tests were made on the capillary blood of sixty-two persons.

HOYER, Cincinnati.

STUDIES IN ASTHMA: THE NOSE AND THROAT IN FIVE HUNDRED CASES OF ASTHMA. F. L. WEILLE, New England J. Med. **215**:235 (Aug. 6) 1936.

Almost one half of the 500 patients were between 30 and 50 years of age. So few children of 10 years of age or less were included that deductions regarding them are worthless.

Sinusitis was seen in 362 of the cases. This frequency should serve to make the rhinologist allergy-minded and the allergist sinus-minded. Severe sinusitis was most frequently observed as a purulent inflammation of an antrum or as ethmoiditis with polypoid degeneration.

Of the 500 patients, 259 had normal tonsils; 186 had chronic tonsillitis, but in only 35 of these was the tonsillitis severe; 119 had had previous tonsillectomy; unfortunately, numerous patients in the latter group had more or less troublesome tonsillar remnants.

Of the 500 patients, 133 had x-ray films of the teeth. In every such case films of all the teeth were taken. In only 84 patients were abscessed teeth discovered, and, of these, only 59 had the abscessed teeth extracted; 39 of the patients were improved or cured, whereas 20 were the same or worse.

A group of 36 patients had bronchoscopy as a part of their treatment; 12 of the patients were improved and 3 were cured; 6 were temporarily cured, but later were the same as before treatment. The remaining ones were not benefited.

It is interesting to observe the results in the asthma in 290 patients who had no form of surgical treatment, whether drainage of sinuses, bronchoscopy, removal of polyps or of teeth, tonsillectomy or other operation. Of these, 142 had slight to severe sinusitis; 15 had pansinusitis; 81 had infected tonsils, and in 20 of these the tonsils were severely infected; 25 had abscessed teeth but were untreated. About two thirds were improved or cured; the remainder were the same or worse.

GENGENBACH, Denver.

CONGENITAL CYSTIC MALFORMATION OF THE LUNG (REPORT OF TWO CASES). VERNON L. PETERSON, West Virginia M. J. **32**:311 (July) 1936.

About seventy cases of congenital cystic malformation of the lung have been reported in the American literature in nine years.

Peterson discusses the etiology, origin, symptoms, differentiation, complications and treatment.

Treatment includes thoracotomy, aspiration, bronchoscopic drainage with instillation of iodized oil, cauterization of communicating bronchi with collapse of the cyst and removal of the lobe.

Two cases are reported. One patient was an infant 1 year old, with a normal history for the first six months. After that there were frequent chest colds, attacks of low grade fever and loss of appetite and weight. Roentgenograms showed an air-containing cyst of the upper lobe of the right lung, with chronic pulmonary infection.

The second patient was a girl 9 years old in whom pulmonary tuberculosis was suspected. There was a history of recurring pulmonary infection, with cough and a moderate amount of sputum. No tubercle bacilli were found. Roentgenograms showed a honeycombed appearance of the entire right lung. A diagnosis of multilocular congenital cyst of the lung was made. The patient being a transient, no further follow up could be made.

SHAWKEY, Charleston, W. Va.

X-Ray Therapy in Bronchitis in Children. Russell C. Bond and Charles H. Clovis, West Virginia M. J. **32**:345 (Aug.) 1936.

The history of the use of roentgenotherapy in disease of the chest is traced briefly.

A series of fifty-nine cases of "chronic cough" treated by roentgen rays is reported.

The importance of case study and selection for roentgen therapy is stressed as is the importance of local treatment, conjointly, for such conditions as sinusitis, tonsillitis and allergic conditions.

The treatment is advised for those cases in which the condition does not respond to the usual methods of treatment. In these cases the cause of the cough is believed to be involvement of the mediastinal, tracheobronchial and peribronchial lymph nodes.

In the fifty-nine cases reported the patients varied from 8 months to 12 years in age and the duration of the cough from one week to five years. All gave a negative reaction to tests with tuberculin.

The technic of the roentgen treatments was carefully controlled by an expert roentgenologist. The average maximum number of treatments was four per patient, at weekly intervals.

The therapy gave good results in fifty-one cases and fair in five and was without benefit in three.

Shawkey, Charleston, W. Va.

Three Cases Illustrating Surgical Treatment of Bronchiectasis in Childhood. R. Wilson and J. A. Carter, Proc. Roy. Soc. Med. **30**:399 (Oct.) 1936.

Bilateral Lobectomy.—A girl of 7 years complained of cough after an attack of measles at the age of 2 and for three years suffered attacks of fever, with expectoration of foul sputum. Bronchography with iodized poppy-seed oil 40 per cent revealed bilateral basal bronchiectasis. Left lobectomy was performed before she left the hospital. Right lobectomy was performed later. Recovery from both operations was uneventful.

Total Pneumonectomy.—A child aged 5 years had pneumonia in 1933 and again in January 1936, and after that suffered from persistent cough. Bronchography with iodized oil showed cylindric bronchiectasis of the left lung, herniation of the mediastinum and narrowing of the left main bronchus. In June left total pneumonectomy was performed. Postoperative pyrexia developed, due to infection of the blood clot.

Left Lower Lobectomy.—A boy aged 8 years had whooping cough in 1933, and for two years he had severe cough with considerable fetid sputum. Bronchography with iodized oil revealed bilateral bronchiectasis, much worse on the left side. Left lower lobectomy was performed, and recovery was uneventful.

The report is accompanied by reproductions of x-ray plates taken after injection of iodized oil.

Williamson, New Orleans.

Secondary Thrush of the Bronchi. J. F. D. Shrewsbury, Quart. J. Med. **5**:375 (July) 1936.

Shrewsbury appears to object to the acceptance of "bronchomoniliasis" as a primary fungous disease of the lungs, as proposed by Castellani.

He says that such a disease does not exist in England, that the fungi which Castellani has called "Monilia" are simply strains of common thrush fungus, that these fungi are frequently present in human sputum, independent of the nature of the primary pulmonary disease, and that secondary thrush infections of the bronchi occur.

Bradford, Rochester, N. Y.

Pneumonia with Late Roentgen Signs. C. Hurmuzache and S. Pineles, Bull. Soc. de pédiat. de Iasi **7**:21 (Jan.-March) 1936.

Two cases of pneumonia are reported in which characteristic roentgen shadows did not appear until after the patients had been ill for six and eight days, respectively.

Leslie, Evanston, Ill.

Migrating Pneumonia. Marie Camner and S. Pineles, Bull. Soc. de pédiat. de Iasi **7**:32 (Jan.-March) 1936.

The authors report a case of migrating pneumonia which lasted twenty-one days.

Leslie, Evanston, Ill.

Treatment of Asthma by Acupuncture. M. Lavergne, Nourrisson **24**:225 (July) 1936.

Acupuncture, as practiced by the Chinese, is recommended for the treatment of asthma in infants. The site for the acupuncture is just below the sternum. Good results are claimed for two thirds of the patients treated.

McClelland, Cleveland.

Unusual Complications of Empyema. Hans Knauer, Arch. f. Kinderh. **106**: 156, 1935.

This is a case report.

Crane, Washington, D. C.

Pneumothorax After Aspiration of a Roasted Coffee Bean or After Its Extraction. S. Kaludjerski, Arch. f. Kinderh. **109**:40, 1936.

A case is reported.

Crane, Washington, D. C.

Bronchographic Diagnosis of Congenital Defects of the Lung. A. Beutel and F. Strand, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:49 (July) 1936.

A 39 year old man had had no previous symptoms of pulmonary disease. Roentgen examination which was carried out because of an injury drew attention to a congenital defect of the left lung. The important bronchographic feature was a broad conical left main bronchus which ended blindly; its smooth, even surface excluded the possibility of an inflammatory or a neoplastic origin. The various types of pulmonary defects are discussed. The bibliography is useful.

McCune, New York.

Recent Bronchographic Results in Dilatation of the Bronchi: V. Bronchiectasis. A. Kautzky, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**: 345 (Oct.) 1936.

This paper provides a useful summary of contemporary opinion concerning divers aspects of the diagnosis of dilatation of the bronchi. Bronchography is not an entirely harmless procedure. Its use is unqualifiedly contraindicated in patients with tuberculosis. Bronchographic diagnosis no longer relates simply to morphologic variation; functional performance must also be taken into consideration. The biliography is copious.

McCune, New York.

Spontaneous Pyopneumothorax and Its Treatment. J. A. Ratner, Vrach. delo **19**:1065, 1936.

Ratner discusses the pathogenesis of spontaneous pyopneumothorax and its treatment. His conclusions are as follows:

1. The necessity of differentiating between acute diffuse pyopneumothorax and the spontaneous circumscribed or encapsulated form must be emphasized. In the former the prognosis is definitely poor, while in the latter it is favorable.

2. The spontaneous diffuse pyopneumothorax requires an early conservative operation (syphon after Buelau). Open pleurotomy in the absence of adhesions and insufficient fixation of the mediastinum is dangerous.

3. In spontaneous circumscribed pyopneumothorax the operation of choice is pleurotomy (thoracotomy). Irrigation of the pleural cavity and active aspiration in spontaneous pyopneumothorax are contraindicated.

4. The practice of performing a conservative operation during the first hours after the appearance of pyopneumothorax is alone able to lower the percentage of mortality in cases of acute spontaneous diffuse pyopneumothorax.

5. In spontaneous pyopneumothorax of tuberculous origin (in most cases, circumscribed) pleurotomy with a subsequent thoracoplasty (when the process is unilateral) is the method of choice.

6. In the tuberculous form of spontaneous pyopneumothorax, the conservative treatment (puncture and oleothorax) is possible only when there is no mixed infection, and this is seldom.

7. Intrapleural adhesions are the main factor in the origin, pathogenesis, course and prognosis of spontaneous pyopneumothorax.

BODER, Los Angeles.

Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

EFFECT OF ACUTE HEMORRHAGE ON THE EMPTYING TIME OF THE STOMACH. E. J. VAN LIERE, C. K. SLEETH and D. NORTHRUP, Am. J. Physiol. **117**:226 (Oct.) 1936.

The emptying time of the stomach was determined on four healthy young adults before and after withdrawal of one tenth of the calculated blood volume. This loss of blood prolonged the emptying time, on the average, 41 per cent. The results indicate that patients who have suffered considerable loss of blood should be given food which is easily digested and which will leave the stomach rapidly.

NOURSE, Cleveland.

ORIGIN OF FECAL FAT IN THE ABSENCE OF BILE, STUDIED WITH DEUTERIUM AS AN INDICATOR. A. SHAPIRO, H. KOSTER, D. RITTENBERG and R. SCHOENHEIMER, Am. J. Physiol. **117**:525 (Nov.) 1936.

The amount of fecal fatty acid has been compared with the amount of dietary fatty acid in two patients with bile fistulas. In the periods when bile did not enter the intestinal tract, the amount of fecal fat was greatly increased. By adding small amounts of deuterium-containing fats to the diet, it was shown that from 65 to 70 per cent of the dietary acids was absorbed in the absence of the bile and that the increase of fecal fat was due to fats secreted into the intestinal lumen.

FROM THE AUTHORS' SUMMARY. (NOURSE, Cleveland.)

ACUTE GASTRO-INTESTINAL DISEASE IN INFANTS. R. M. SMITH, New England J. Med. **215**:701 (Oct. 15) 1936.

Decreasing morbidity and mortality have shown the influence of better artificial feeding, better general care and the use of pasteurized milk. It is interesting to compare the fall in the rate of infant mortality, especially in respect to gastro-intestinal diseases, with the extension in the pasteurization of milk. The two lines run very nearly parallel.

When an infant is taken sick with vomiting or diarrhea or both, or fails to make satisfactory progress in weight, one may reasonably expect to find one of four things: infection somewhere in the body, not necessarily or most likely in the gastro-intestinal tract; a congenital anomaly, again not necessarily in the

gastro-intestinal tract; faulty environment or hygiene; improper food. Treatment to be effective must be directed toward removal of the cause.

GENGENBACH, Denver.

SURGICAL DISEASES OF THE ALIMENTARY TRACT IN INFANTS. W. E. LADD, New England J. Med. **215**:705 (Oct. 15) 1936.

Many an abdominal examination is made valueless by first gagging an infant with a throat stick. Everything that it is possible to learn by inspection should be noted first. In making the abdominal examination, distention, engorgement of the abdominal veins, visible peristalsis or tumor should be looked for before the infant is touched. Gentle palpation must precede deep palpation. Percussion and auscultation should be included, and finally, if the investigation is to be complete, a rectal examination should be made.

Of the diseases requiring surgical attention congenital hypertrophic pyloric stenosis is one of the commonest. In 620 cases, this condition was found to occur more commonly in boys in the proportion of 85 per cent boys to 15 per cent girls. The symptoms usually start in the third week of life, though in 10 per cent of the patients they started in the first week. The treatment is surgical and includes special attention to preoperative care and postoperative feeding. The operation of choice is pyloromyotomy.

In the first 125 cases 13 deaths occurred, a mortality of approximately 10 per cent, while in the next 495 cases the mortality dropped to 4 per cent, and in the latter group 160 patients were operated on consecutively without a fatality.

When vomiting takes place in the first few days of life, and the vomitus contains bile, one should think at once of some form of arrested development of the alimentary tract, causing obstruction below the ampulla of Vater. Such congenital atresia or stenosis may take place in any part of the intestine or may be multiple. In a series of 53 cases at the Children's Hospital, not including cases of obstruction of the sigmoid or rectum, obstruction occurred in the duodenum in 9, in the jejunum in 7 and in the ileum in 31, and in 6 cases the obstruction was either multiple or involved the colon. The mortality in these conditions is extremely high, but the percentage of recoveries is increasing. In this series of 53 patients, 10 survived.

The cases classified as instances of extrinsic obstruction are those in which the condition is dependent on a faulty rotation of the midintestine. They all have in common the lack of the normal oblique attachment of the mesentery of the small intestine and the normal attachment of the mesentery of the ascending colon. The volvulus usually twists in a clockwise direction, though occasionally it goes in the reverse direction. It has been found inadequate to reduce the volvulus only. This has been invariably followed by recurrence or a fatal termination or both.

Intussusception is certainly one of the most important forms of obstruction. The peak of incidence is in the seventh month of life. The disease occurs most commonly in well nourished, healthy-looking babies. The onset is sudden, characterized by crying, evidence of abdominal pain, pallor, nausea and vomiting. The treatment is surgical. In this series of 431 cases, 32 patients were operated on in the period from 1908 to 1912, 18 of whom died—a mortality of 59 per cent. From 1912 to 1928 the statistics have consistently improved, and in the period from 1928 to 1936, 149 patients were operated on, 21 of whom died—a mortality of 14 per cent. A high temperature and other evidences of severe toxemia usually follow the reduction of intussusception. The administration of dextrose intravenously and of saline solution by clysis appears to be the most successful means at one's disposal for combating this toxemia. In this group of 431 cases there have been 8 recurrences.

GENGENBACH, Denver.

PARTIAL THORACIC STOMACH, WITH REPORT OF A CASE. G. RONALD ELLIS, Brit. M. J. **2**:13 (July 4) 1936.

Ellis reports a case of partial thoracic stomach.

ROYSTER, University, Va.

MALROTATION OF THE INTESTINES IN A CHILD AGED NINE MONTHS; CURED BY OPERATION. R. H. DOBBS and K. HERITAGE, Proc. Roy. Soc. Med. **30**:404 (Oct.) 1936.

A case is reported in a boy of 9 months, who was admitted to the hospital on account of repeated vomiting during the previous few days. For the first three days of life he had vomited everything, but the vomiting soon lessened, and he was fed on the breast for seven months but could never take more than 3 ounces (90 cc.) at one feeding. He was then put on cow's milk and a general diet, and after that he had frequent attacks of vomiting, in spite of which he progressed well. Two days before admission he commenced to vomit everything, including water, and became constipated. After roentgen examination following a barium sulfate meal, a provisional diagnosis of duodenal stenosis was made. Laparotomy was performed under local anesthesia, and malrotation of the intestines was found. Details of the operation are given in the report, with pictures to illustrate the condition. The patient made an uneventful recovery.

WILLIAMSON, New Orleans.

BILIARY CIRRHOSIS WITH CYANOSIS AND FINGER-CLUBBING. P. R. EVANS, Proc. Roy. Soc. Med. **30**:406 (Oct.) 1936.

A case was reported in a girl of 12 years. In 1932 she commenced having attacks of jaundice, with pale stools and dark urine, at which times she would vomit for several weeks. Enlargement of the abdomen was noticed at this time. The liver was found to be 2 fingerbreadths below the costal margin; the spleen was just palpable. In 1934 she began to have acute hematuric nephritis with ascites and bilateral hydrothorax, and eleven months later she became dyspneic on exertion and showed marked cyanosis of the nails, tongue and lips. The fingers by this time were clubbed.

The history and the results of the laboratory examinations are given in detail. The report is accompanied by a picture of the patient with the liver and spleen marked out, and a picture of the hands and feet, which shows the clubbing of the fingers and toes.

WILLIAMSON, New Orleans.

HEPATO-SPLENOMEGALY; ? IDIOPATHIC CIRRHOSIS. C. T. POTTER, Proc. Roy. Soc. Med. **30**:409 (Oct.) 1936.

A case was reported in a girl of 5 years. Five days before admission to the hospital she had severe pain in the epigastrium that lasted only a very short time, and in the following five days she had intermittent epigastric pain of a milder nature. On examination a large tumor in the abdomen was found, and bruises about the body were noticed. The mother claimed that the child had had a tendency to bruise ever since she was an infant. The report includes the past history, the family history and the results of physical examination, of investigations of the blood, urine and material obtained by splenic puncture and of roentgen examination of the long bones.

WILLIAMSON, New Orleans.

EARLY ALIMENTARY HYPOGLYCEMIA, OR PREHYPERGLYCEMIA, IN CHILDREN. E. BENVENUTO, Riv. di clin. pediat. **34**:632 (July) 1936.

Of ten infants and sixty older children up to the age of 12 years Benvenuto observed that thirty, or 42 per cent, showed the presence of early alimentary hypoglycemia. This hypoglycemia appeared within the first ten minutes after the ingestion of 1 Gm. of dextrose per kilogram of body weight. It would then be followed by the usual rise in blood sugar noted after the ingestion of dextrose. The blood sugar varied in amount from as low as 0.006 per cent to as high as 0.057 per cent. Benvenuto expresses the belief that the hypoglycemia depends on a reflex stimulation of the regulators of blood sugar, which in certain children are not in perfect functional equilibrium.

HIGGINS, Boston.

USE OF MATERNAL BLOOD IN THE TREATMENT OF SEVERE VOMITING IN THE BABY. E. JUJOY, Med. de los niños **37**:167 (June) 1936.

Biweekly injections of 20 cc. of citrated maternal blood into the gluteal region have proved very beneficial in severe vomiting, especially in that due to pyloric obstruction in which surgical intervention would involve too great a risk. The theory on which this procedure is based is not clear. In three of the ten cases in which it was tried, only one injection was necessary.

DWYER, Kansas City, Mo.

A CASE OF FETAL HERNIA. W. V. CARUSO, Arch. de pediat., Rio de Janeiro **9**:23 (Oct.) 1936.

Photographs are shown of a large umbilical hernia containing viscera in considerable quantity. Operation was performed at once, but the child died in twenty hours.

SANFORD, Chicago.

BANANA TREATMENT FOR INFANTILE DIARRHEA. R. DE AMORIM, J. de pediat., Rio de Janeiro **3**:463 (Oct.)) 1936.

Powdered banana was given to ninety-seven infants for dystrophies marked by diarrhea. The fruit was given every three hours and gave successful results in from twenty-four to seventy-two hours.

SANFORD, Chicago.

ROENTGEN DIAGNOSIS OF CONGENITAL ANATOMIC AND FUNCTIONAL STENOSIS OF THE LARGE INTESTINE. F. WINDHOLZ, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:282 (Sept.) 1936.

A case of congenital stenosis of the large intestine is described. The diagnosis was made by roentgen examination when the infant was 6 weeks old. Autopsy showed the stenosis to be due to adhesions, which were presumably caused by fetal peritonitis. In order to demonstrate stenosis in this region, it is necessary to compare the results obtained with partial and with complete filling of the colon. The value of the combined method of examination is demonstrated in a case of congenital megalocolon associated with situs inversus viscerum. Complete filling with opaque material revealed no abnormalities in the appearance of the large intestine. However, when only a small amount of contrast medium was introduced, the presence of functional stenosis of the colon became apparent.

MCCUNE, New York.

HEPATOMEGALY WITH DISTURBANCE OF THE CARBOHYDRATE METABOLISM. GEORG OSKAR HARNAPP, Monatschr. f. Kinderh. **66**:169 (July) 1936.

In this and in the two following articles Harnapp submits case reports of different types of enlargement of the liver. The first two illustrations are examples of von Gierke's disease. Characteristic of this are low blood sugar, ketonuria without glycosuria, abnormal carbohydrate reactions following the administration of epinephrine, unusual curves of sugar tolerance and hypersusceptibility to insulin. Clinically, the condition is characterized by an early beginning and the absence of icterus, ascites and splenic enlargement. The general condition is good, and there is no increase in the amount of bile excreted in the urine. A biopsy showed the typical pathologic changes of von Gierke's disease.

In other cases reported he found that children with exactly the same clinical symptoms showed unquestionable cirrhosis of the liver at biopsy.

In a final paper discussing the significance of these case reports he concludes that there is no symptom pathognomonic of von Gierke's disease. The most reliable methods in diagnosis are to follow the simple clinical signs, such as enlargement of the liver often dating back to birth, tendency to accumulation of fat and good general condition.

GERSTLEY, Chicago.

Relation Between Diminished Absorption of Vitamin C and Pathologic Pigmentation in Gastro-Enteritis and Achylia Gastrica. H. Schroeder and M. Einhauser, München. med. Wchnschr. **83**:923 (June 5) 1936.

The athors studied the disturbance in pigment metabolism in patients with chronic gastro-enteritis. The absorption of vitamin C is diminished in the presence of the abnormal intestinal flora encountered in some cases of chronic gastro-enteritis. The least absorption of vitamin C was found in patients with achylia gastrica. Good results were obtained in patients with abnormal pigmentation of the skin by parenteral administration of vitamin C.

Deficiency in vitamin C can be due to (1) lack of a sufficient quantity in the diet, (2) diminution in the absorption of the vitamin from the gastro-intestinal tract and (3) an increase in the requirement, as in infectious diseases, tuberculosis and carcinoma.

Brahdy, Mt. Vernon, N. Y.

Congenital Atresia of the Esophagus. M. Simonsen, Röntgenpraxis **8**:531 (Aug.) 1936.

A 4 day old infant regurgitated all feedings from the time of birth. Roentgen examination with a contrast medium revealed congenital atresia of the esophagus at the juncture between the proximal and medial thirds. Injection of an opaque medium by means of a gastrostomy tube revealed the presence of a fistula between the lower segment of the esophagus and the trachea, and another between the trachea and the upper segment of the esophagus. The contrast medium so instilled filled the bronchial tree, entered the upper segment and finally appeared in the infant's mouth.

McCune, New York.

Stenosis of Bile Ducts. S. D. Poesponegoro, Maandschr. v. kindergeneesk. **6**:67 (Nov.) 1936.

This is a description of two cases. In the first one, which was observed in a girl, there appeared, after death at the age of 7½ months, to be atresia of the bile ducts; in the second one, which was observed in a boy, there was found, after death at the age of 8 months, real stenosis of a bile duct.

van Creveld, Amsterdam, Netherlands.

State of Health of Children Who Have Suffered from Pylorospasm. J. C. Schippers and H. J. van der Molen, Maandschr. v. kindergeneesk. **6**:83 (Dec.) 1936.

In the authors' clinic from 1912 to 1936, 211 children with pyloric stenosis were treated, some conservatively (mean number of days' stay in the hospital, ninety) and some, after 1921, operatively (mean number of days fifty). Of the surviving children, the fate of 132 could be examined. Of these, 34 per cent had become highly nervous, and 18.3 per cent continually complained of disturbances of the digestive tract. In the authors' opinion, pyloric stenosis should be looked on as a manifestation of a less favorable constitution.

van Creveld, Amsterdam, Netherlands.

Nervous Diseases

Extensive Pigmented Nevus Associated with Primary Melanoblastosis of the Leptomeninges of the Brain and Spinal Cord. E. W. Netherton, Arch. Dermat. & Syph. **33**:238 (Feb.) 1936.

The similar ectodermal origin of skin and nerve tissue suggests that both may suffer developmental anomalies from common or analogous developmental defects. The occasional association of mental deficiency and neurofibromatosis is cited as an instance. Melanoma of the meninges, however, is usually of metastatic

rather than of developmental origin; a case illustrating the rare coincidence of primary melanoblastosis of the meninges and a pigmented nevus is presented. A youth aged 17 complained of headache, blurred vision, vomiting and defects of memory. He had 4 or 5 diopters of swelling of the optic disk a large hairy nevus over the face, neck and scalp and smaller nevi over the body. Two operations were performed; suboccipital craniectomy—which revealed a bluish gray mantle over the posterior surface of the medulla, resembling a venous angioma—and cervical laminectomy. The latter revealed that the cord was completely covered by a bluish gray sheath, which at autopsy was seen to be a cylinder of tumor tissue replacing the pia-arachnoid. The cells of this mass had oval vesicular nuclei; scattered throughout them were numerous irregular elements containing coarsely granular yellowish brown pigment. Mitosis was infrequent. The pia of the medulla was similarly involved. The whole picture indicated diffuse melanoblastosis of these meninges.

The superficial portion of the nevus consisted of cells containing inadequate quantities of protoplasm and chromatin, while all through the mass were large multinucleated cells and others containing coarsely granular pigment. The picture was that of the "giant neuronevus of the scalp" described by Masson. In discussing the relationship of the nevus to the meningeal anomaly, Netherton suggests three possibilities: (1) that the meningeal melanoma is metastatic, (2) that the two sets of tumors are unrelated and exist only by coincidence and (3) that they are both the product of widespread ectodermal developmental disturbance. The last explanation appears to be the most reasonable, and Netherton suggests that a lesion of this type may be considered as filling the gap between extensive benign melanoma of the skin and primary melanotic tumor of the meninges.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

PYKNOLEPSY. JOSEPH L. ABRAMSON, J. Nerv. & Ment. Dis. **82**:249 (Sept.) 1935.

Friedman in 1906 first called attention to a symptom complex resembling petit mal, occurring in children between the ages of 4 and 12 years. He called it a disease entity. There is a cyclonic onset, with "heaping up" or development of the maximum number of daily attacks at once. They occur from ten to a hundred times daily over weeks, months or years and are not influenced by drugs. Clonic movements and urinary incontinence are rare. No biting of the tongue or frothing at the mouth is observed.

After the report of three cases of this condition, Abramson gives considerable thought to the controversy in the literature as to whether pyknolepsy is a disease sui generis or a symptomatic variation of the paroxysmal reaction, and he reaches the opinion that it is not a disease entity with a specific etiology but "a type of reaction of the nervous system." A review of the literature suggests a good prognosis, with disappearance of the attacks at puberty. In one of the author's cases four months of intensive analytic therapy resulted in no improvement.

HART, New York. [ARCH. NEUROL. & PSYCHIAT.]

GLIOMA OF THE AQUEDUCT OF SYLVIUS. W. V. CONE and JEAN SAUCIER, Union méd. du Canada **65**:450 (May) 1936.

A boy of 11 years began to show trembling and irritability. This was diagnosed and treated as chorea. There was no involvement of cranial nerves. A year later he began to have intense headaches, vomited frequently and had an unsteady gait. His head was enlarged. The pupils were dilated and reacted only feebly. Papilledema was present. Ventriculograms showed marked hydrocephalus. The intracranial pressure was equivalent to that of 700 mm. of water. The protein in the ventricular fluid was 30, and that in the lumbar fluid 70, mg. per hundred cubic centimeters. The preoperative diagnosis was that there was a tumor at the midline in the posterior fossa.

Operation revealed a tumor of the fourth ventricle, which was removed and proved to be an astrocytoma. The boy's convalescence was slow, being com-

plicated by strabismus and difficulty in speech and in gait. These slowly cleared up, and he returned to school, where he is doing normally.

The authors point out that so much damage in an adult would undoubtedly have left a residuum.

DAFFINEE, Boston.

MECHANISM OF INTERNAL HYDROCEPHALUS IN SPINA BIFIDA. DOROTHY S. RUSSELL and CHARLES DONALD, Brain **58**:203, 1935.

The frequent association of hydrocephalus with spina bifida has been observed for centuries, but no explanation of this association has yet proved generally acceptable. Russell and Donald offer a mechanical explanation of the production of communicating hydrocephalus in a series of cases of meningomyelocele. Ten cases were studied. Internal hydrocephalus was present at birth in all but two instances. Of the eight cases in which hydrocephalus was present, two were of the noncommunicating type and three of the communicating type, and in the three remaining cases the type was not determined. In all ten cases a remarkable malformation of the hindbrain was observed. A tongue of variable length, consisting of cerebellar tissue and the greatly elongated medulla oblongata, protruded downward into the spinal canal. It overlapped and compressed the upper segments of the cervical portion of the cord, distending the dural theca in this neighborhood and filling the foramen magnum. The cavity of the fourth ventricle extended ventrally into this tongue, lying between the cerebellar and the medullary component. The spinal cord appeared abnormally small, and the cervical roots always ran in a cephalic direction to reach their exits through the dura mater. Hydromyelia was commonly present in a variable number of consecutive segments in the cervical and thoracic portions of the cord. There was conspicuous hypoplasia of the cerebellum. The pons and the cranial nerve roots arising from the pons and the medulla were greatly elongated.

This curious maldevelopment was first described by Arnold (1894) and was subsequently studied by Chiari (1895), Solovtzoff (1901) and Gredig and Schwalbe (1907), the last-named authors describing it as the Arnold-Chiari malformation.

The relation of the malformation to hydrocephalus is explained as follows: The elongated fourth ventricle extends for a considerable distance below the foramen magnum; it follows that if the foramina of Luschka and Magendie are patent, the cerebrospinal fluid escapes into the subarachnoid space within the vertebral canal. The plugging of the upper cervical part of the canal by the Arnold-Chiari malformation is likely to hinder any upward flow of fluid into the subarchanoid channels within the posterior fossa, into which it passes normally on its way to escape through the cranial arachnoid villi. According to the experiments of Dandy and Blackfan, the greater proportion, from three-fourths to four-fifths, of cerebrospinal fluid is absorbed from the surface of the brain, and from one-fourth to one-fifth only, from the spinal canal. If this estimate is accepted, it follows that occlusion of the foramen magnum in cases of spina bifida will lead to damming back of cerebrospinal fluid in the ventricular system and hence to internal hydrocephalus. Evidence can be advanced in support of this hypothesis. In two cases in which death was imminent, a suspension of india ink was introduced into the lateral ventricles, and the distribution of the particles was examined at necropsy. There was a profuse deposit of pigment throughout the ventricular system and in the subarachnoid space of the spinal canal below the level of the Arnold-Chiari malformation. Above this level a very small or moderate amount was visible at the base of the brain and a very little in the sulci over the cerebral convexities. In two other instances there was ascending purulent leptomeningitis with pyocephalus following infection of the tissues at the site of the spinal defect. Examination showed severe purulent infiltration of the spinal meninges up to the level of the Arnold-Chiari malformation, but above this level the inflammatory reaction was confined mainly to the ventricular system, where conspicuous pyocephalus was present.

Hydrocephalus has also been observed in some cases of meningomyelocele. Russell and Donald studied a case in which there was no associated hydrocephalus.

In this case a type of malformation similar to that described in the cases of meningomyelocele with hydrocephalus was presented, but to a far less severe degree. This suggests the possibility that greater degrees of the malformation may cause the hydrocephalus which complicates meningomyelocele in some instances.

Examination in two cases of spina bifida occulta in which hydrocephalus was absent disclosed no abnormality in the brain stem.

SALL, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

EFFECT OF INCREASED INTRACRANIAL VENOUS PRESSURE ON THE PRESSURE OF THE CEREBROSPINAL FLUID. T. H. B. BEDFORD, Brain **58**:427, 1935.

Numerous conflicting opinions have been expressed concerning the normal relation of the intracranial venous and the cerebrospinal fluid pressure. Some have concluded that the two pressures are equal (Hill, and Frazier and Peet); others have expressed the belief that the spinal fluid pressure is the greater. Weed and Hughson (1921 and 1922) concluded that normally the cerebrospinal fluid pressure is always higher than the torcular pressure. This finding was confirmed by Bedford, who found the torcular pressure to be from 25 to 95 mm. of a 4 per cent solution of sodium citrate below that of the cerebrospinal fluid pressure.

That constriction of the veins of the neck is followed by increase in the pressure of the cerebrospinal fluid has been known for some time. Increased production or decreased absorption of cerebrospinal fluid has been offered as an explanation for the change in pressure. Becht found that it is due to an accumulation of venous blood in the cranial cavity and displacement of cerebrospinal fluid into the spinal canal. These observations were confirmed and extended by Weed and his co-workers (1933).

Although the effect on the cerebrospinal fluid pressure of an abrupt and temporary increase in the intracranial venous pressure seems to have been determined with accuracy, little or no work is available on the influence of a prolonged state of raised intracranial venous pressure. It is with this idea in mind that Bedford's experiments were performed. Dogs were used.

The effect of temporary occlusion of the external jugular veins on the pressure of the cerebrospinal fluid and the venous pressure at the torcula was studied. It was found that the cerebrospinal fluid and the torcular pressure attained their maximum heights simultaneously within a few seconds after the veins were occluded. On release of the jugular veins, the pressures returned to their original levels within a few seconds. It was found that after occlusion of the jugular veins the two pressures might rise to nearly the same level. The average proportion of the increase of venous pressure which was reflected in the pressure of the cerebrospinal fluid was 61 per cent.

The effect of prolonged occlusion of the external jugular veins in dogs resulted usually in a fall of the cerebrospinal fluid and torcular venous pressures soon after they attained their maximum height. The cerebrospinal fluid pressure at first falls rapidly and then more gradually, the fall often taking place in a steplike manner. A level approximating the original pressure before the veins were ligated is usually attained after from thirty to forty-five minutes. The pressure then remains steady or continues to fall somewhat below its original level. The fall in the venous pressure is not as rapid or complete. By the time the cerebrospinal fluid pressure has returned to normal, the venous pressure is still several times its normal height, but it drops to normal after some time. Occlusion of the lateral sinuses midway between the torcula and the point at which they are joined by the basal veins resulted in pressure changes similar to those following ligation of the external jugular veins.

The sudden rise of cerebrospinal fluid pressure which follows venous obstruction is generally regarded as due to direct influence of the raised intracranial venous pressure on the cerebrospinal fluid pressure and not to increased formation of cerebrospinal fluid. Bedford's experiments indicate that a high torcular venous pressure of several hours' duration is not followed by increased formation of cerebrospinal fluid.

Although it is impossible to be certain of the effect of pressure changes at the torcula on the capillary pressure of the choroid plexuses, it is possible that they are closely related. These experiments indicate that the formation of cerebrospinal fluid is not influenced by changes in the venous pressure of the galenic system and favor the view that the process is secretion rather than simple filtration.

As regards the cause of the fall in pressure, it seems probable that the venous pressure falls mainly on account of the development of collateral circulation, and this is responsible indirectly for part of the fall in the pressure of the cerebrospinal fluid. The occurrence, however, of a normal cerebrospinal fluid pressure in the presence of a torcular venous pressure which is several times its original height and the phenomena observed when the external jugular veins are released after obstruction of several hours' duration suggest that there is an actual decrease in the total volume of cerebrospinal fluid.

SALL, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

FAMILIAL CONGENITAL BOURNEVILLE'S DISEASE (TUBEROUS SCLEROSIS) ASSOCIATED WITH SYMPTOMS OF NEUROFIBROMATOSIS (RECKLINGHAUSEN'S DISEASE). L. BABONNEIX, M. BRISSOT, MISSET and DELSUC, Ann. méd.-psychol. (pt. 2) **94**:102 (June) 1936.

Two brothers, 6 and 4 years of age, had severe mental defect, epilepsy and characteristic facial nevi associated with congenital anomalies of the skin resembling those observed in Recklinghausen's neurofibromatosis. The eyegrounds showed no congenital lesions. Both maternal grandparents were mentally deficient. The grandfather was alcoholic and died at the age of 41. Roentgenograms of the skulls of the patients showed intracranial calcifications which suggested tumor. The authors stress the familial occurrence of tuberous sclerosis and its coincidence with neurofibromatosis. These two cases support Bielschowsky's thesis that tuberous sclerosis and neurofibromatosis represent different aspects of the same congenital disease.

YAKOVLEV, Waltham, Mass. [ARCH. NEUROL. & PSYCHIAT.]

PSEUDOMYOPATHIC POLYNEURITIS. GRAÇOSKI and HURMUZACHE, Bull. Soc. de pédiat. de Iasi **6**:71 (Oct.-Dec.) 1935.

A boy 7 years old suffered from polyneuritis, which in symptoms resembled progressive muscular atrophy. However, a favorable evolution with disappearance of the symptoms made the authors reject the diagnosis of myopathy in favor of that of polyneuritis.

LESLIE, Evanston, Ill.

SYDENHAM'S CHOREA CURED BY INJECTIONS OF SODIUM SALICYLATE. S. GRAÇOSKI and MARIE CAMNER, Bull. Soc. de pédiat. de Iasi **7**:10 (Jan.-March) 1936.

A child 4 years old suffered from severe chorea which was intractable to the usual arsenicals. Recovery followed five intravenous injections of sodium salicylate (6 mg. per day).

LESLIE, Evanston, Ill.

PHYSIOPATHOLOGIC CHANGES IN INTRACRANIAL PRESSURE ASSOCIATED WITH PRODUCTION AND RESORPTION OF CEREBROSPINAL FLUID. RISER, Encéphale **30**:685, 1935.

The experimental and clinical observations which constitute a large part of the data on which this report is based have been collected since 1920. The methods used included simultaneous measurement of the spinal or intracranial pressure and the pressure in the large veins and retinal and systemic arteries, direct examination of meningeal and cortical vessels as carried out by Donders and Forbes and perfusion of the brain, either in situ or when isolated. The aneroid manometer of Mainini, which permits readings of positive and negative pressure, was often used.

The main causes of variation in intracranial pressure are the almost complete rigidity of the craniovertebral casing, the incompressibility of the nerve tissue

and its envelops, the volume of cerebrospinal fluid and the quantity of blood circulating in the craniovertebral cavity. The effect on intracranial pressure of various liquids injected into the general circulation is explained chiefly by the osmotic tensions of these liquids in keeping with the work of MacKibben and Weed. The theory of Barré and Klein that only the temperature, not the molecular concentration, of the injected fluid is effective is not accepted. The thermal effects were slight and transitory. The study of the production and resorption of the cerebrospinal fluid is beset with difficulties. Foreign substances introduced into the spinal fluid can be followed into the blood or the lymphatic circulation. These experiments, from which most explanations of the resorption of the spinal fluid have been derived, tell nothing about its destiny. They give information only concerning the evacuation of foreign substances. The one fact which proves that spinal fluid is produced is that internal hydrocephalus results from ventricular block and that the hydrocephalus disappears when the obstacle is removed. The overproduction of fluid in forced drainage by the Kubie method was confirmed by Riser, Plangues and Simovici, but there is no evidence for tissue drainage or for the therapeutic effects claimed. Normal renewal of the spinal fluid seems to exist, but it is slow.

The various hypotheses concerning the site of production and resorption are considered: The theory of Monakow—production by the blood vessels and epithelium of the choroid plexus, diffusion between the ependymal cells and through the parenchyma and absorption by the parenchyma and the meninges—has no evidence in its favor. The theory of Hassin of extraventricular production of spinal fluid and absorption by the choroid plexus cannot be accepted, for it does not explain the internal hydrocephalus following mechanical block. The production of spinal fluid by the choroid plexus seems demonstrated, principally by the results of destroying the plexus. The ubiquitous production by the parenchyma and the direct evacuation to the meninges are possible but have not been demonstrated. This mechanism may coexist with production in the plexus. Riser suggests that the plexus may be the essential source, functioning in rapid episodic production of fluid. The site of absorption remains obscure. The existence of a "one way current" from the ventricles to the meninges appears certain.

Many facts point to the following conclusions concerning the relation between passive circulatory changes and spinal fluid pressure: Arterial hypertension, constant or paroxysmal, has little effect on the spinal fluid pressure. Venous hypertension, either local or general, always gives rise to hypertension of the spinal fluid. However, the relation between these two factors is not mathematical. Stimulation of the sympathetic nervous system, either directly or by epinephrine and other drugs, produced no change in cerebrospinal pressure, except so far as there were secondary vagal effects. Stimulation of the vagus nerve resulted in increased pressure, which is explained by the venous hypertension. There is no evidence of any direct effect on the production of fluid or the cerebral circulation. There is no evidence of the existence of an apparatus regulating craniovertebral pressure and cerebral vasomotility in the higher vertebrates. The contractility of the cerebral arteries is limited.

The main factors resulting in pathologic intracranial hypertension are: meningeal lesions with congestion of the choroid plexus and overproduction of spinal fluid, perhaps also with interference with venous absorption in cases of septic meningitis; tumor, in the broadest sense of the word; general or jugular venous hypertension; toxic factors, such as those resulting from renal retention, and mechanical irritation, as in trauma or operation. The action of the last two factors is not clear. Suppuration of the central nervous system, as long as it is distant from the meninges, is peculiarly torpid. Hypertension is slight and always appears late unless the abscess blocks the ventricles mechanically. Chronic aseptic degenerative parenchymatous lesions, such as multiple sclerosis, do not involve any notable evacuation of degenerative products toward the meninges. Their effect on cerebrospinal fluid pressure is absent or slight. Acute aseptic degenerative lesions, such as softening, can result in transitory hypertension. Any lesion, whatever its nature, which blocks the evacuation of fluid from the ventricles results in

internal hydrocephalus, but the mechanism of communicating hydrocephalus is obscure. The favorable results obtained by Putnam from endoscopic coagulation of the choroid plexus point to hypersecretion of fluid by the plexus.

Hypotension of the cerebrospinal fluid seems to have little or no ill effects when it is permanent, but sudden, episodic hypotension, as in trauma, constitutes a definite syndrome. Thus, Leriche has observed the depression of a cranial scar accompanied by intense headache and an increase in the number of epileptic seizures.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

NERVOUS CRISES AND LOSS OF CALORIC RESPONSE (VESTIBULAR) AS SIGNS OF A TUMOR OF THE FOURTH VENTRICLE. J. A. BARRÉ, JEAN MASSON and A. CHARBONNEL, Rev. neurol. **64**:742 (Nov.) 1935.

A 6 year old boy had falling spells, epigastric pain, dizziness, pallor, vomiting and headache. Vestibular tests showed complete loss of caloric response. There was cerebellar dysfunction on the left side. No auditory loss could be demonstrated. The tumor was successfully removed. It obliterated the aqueduct of Sylvius and enveloped the right lobe of the cerebellum.

DAFFINEE, Boston.

PROGRESSIVE SYMMETRICAL FAMILIAL CENTROLOBAR LEUKO-ENCEPHALOSIS (SCHILDER'S DISEASE). C. JAKOB and T. GONZÁLEZ, Arch. argent. de neurol. **14**:51 (March-April) 1936.

Jakob and González describe three cases of progressive diffuse sclerosis of the familial juvenile type (familial progressive leukodystrophy). In three brothers the same morbid process appeared in the same epoch of life—between 6 and 10 years of age. Anatomic studies showed subcortical and symmetrical demyelinization of the white substance of the centrum ovale, with destruction of the myelin sheaths and axis-cylinders, accompanied by a glial reaction, and sparing of the arcuate fibers. The lesions were degenerative.

ALPERS, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

ROENTGENOSCOPIC EXAMINATION OF THE VENTRICULAR CAVITIES WITH IODIZED OIL. (ROENTGENODOVENTRICULOSCOPY.) R. CARRILLO and J. ALBERTO AGUIRRE, Arch. argent. de neurol. **14**:77 (March-April) 1936.

In iodoventriculography 4 cc. of iodized poppy-seed oil 40 per cent is injected, but when there is advanced internal hydrocephalus, as much as 8 or 10 cc. is used. Carrillo and Aguirre think that it is possible to follow in the roentgenoscopic plate the displacement of the opaque substance, to establish the form of the ventricles and especially to determine block by means of fluoroscopic examination. Roentgenoscopy at present is only a complement to iodoventriculography. Fluoroscopic visualization of the ventricles with iodized poppy-seed oil produces less distress in the patient than air and permits easy diagnosis of ventricular block.

ALPERS, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

OCCURRENCE OF EPIDEMIC ENCEPHALITIS COMBINED WITH MULTIPLE SCLEROSIS. GERD PETERS, Deutsche Ztschr. f. Nervenh. **138**:23 (Aug.) 1935.

Attention has been called of late to the relative frequency of encephalitic symptoms in cases of multiple sclerosis. The difficulty of differential diagnosis, especially in the early stages of acute multiple sclerosis, has been pointed out by Guillain, Marburg and Redlich. However, none of the authors assumed the presence of a combination of the two diseases. Peters reports a case which seems to indicate that such a combination may take place.

A boy at the age of 6 suffered an attack of encephalitis, which left him with mental backwardness. Three years later a diagnosis of postencephalitic "pseudopsychopathy" was made in a psychiatric clinic. Muscular rigidity with salivation

gradually supervened. At the age of 19, temporary paresis of the lower portion of the right arm set in. At the age of 20, the patient died of chronic parkinsonism.

There was a typical histologic picture of epidemic encephalitis. The substantia nigra showed glial fibrosis, with nearly complete destruction of the myelin of the ganglion cells. There were diminution in the number of ganglion cells in the locus caeruleus and an increase in glia at the base of the fourth ventricle and in the aqueduct, all of which speaks for epidemic encephalitis. In addition, there were sharply circumscribed demyelinated areas—some periventricular, some in the white substance and some passing into the outer surface of the cortex. These recent lesions appeared to be typical of multiple sclerosis.

Although a clinical diagnosis of multiple sclerosis was hardly possible in this case, pathologically the circumscribed lesions must be considered as distinct from those responsible for the encephalitis. Peters, therefore, thinks that two distinct processes took place in this case: encephalitis, followed by multiple sclerosis.

BERNIS, Buffalo. [ARCH. NEUROL. & PSYCHIAT.]

PSYCHOLOGIC STATE OF CHOREIC PATIENTS. WOLFGANG HOCHHEIMER, J. f. Psychol. u. Neurol. **47**:49, 1936.

Hochheimer studied in detail the mental condition of six patients with Huntington's chorea, three of whom were in the early stages of the disease and three in far advanced stages. In the early stages the diagnosis of a specific dementia could readily be established. The dementia was characterized by the inconstancy of its manifestations. There were periods, varying in duration, during which the patients succeeded well; they could express themselves and apparently could think correctly. They were by no means devoid of all "intelligence"; they could size up a situation and had good insight. Not until the last stages of the disease did the dementia and intellectual defects become complete.

In patients with far advanced chorea, speech was greatly impoverished and was abrupt, poorly articulated and telegraphic. An attempt to speak for any length of time was associated with such difficulties in articulation that speech became utterly unintelligible. When these patients were requested to repeat what they had said, they became irritable and merely shouted out the same words more loudly, without rendering themselves more intelligible. The more they were urged to express their thoughts in language, the more mute they became. Occasionally they attempted to extricate themselves from the dilemma by confabulation and circumlocution. In this struggle to make themselves understood, they lost the trend of thought and wandered into other spheres of thought wholly irrelevant to the subject-matter to which their attention had originally been directed. Some of the patient's answers to questions were characterized by a certain amount of stereotypy and substitution of words.

In both groups of patients it was evident that there was marked disturbance of all motor and thinking processes. In the final stages of the disease there was loss of orderly continuity of thought, speech and action, so that adequate contact with the outside world was entirely severed. The patients' interests in life became progressively narrower and were finally reduced to the lowest primitive animal life. The dementia became complete.

KESCHNER, New York. [ARCH. NEUROL. & PSYCHIAT.]

HEREDITARY FACTOR IN EPILEPSY. KLAUS CONRAD, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:271 (July) 1935.

Conrad presents evidence to support the hypothesis that there is a significant hereditary factor in epilepsy. He obtained definite information regarding the existence or nonexistence of twins among 12,561 epileptic patients who were inmates of various German institutions on Feb. 1, 1934. This cross-sectional method of studying the problem was preferred to that of collecting material over a long period. It avoids a number of errors, such as counting the same patient twice, difficulty in finding relatives and inaccuracy of records. There were 258

pairs of twins in which one of the pair suffered from epilepsy. The incidence of twin birth among epileptic patients was 1 : 48.6, as compared with 1 : 60.6 for the population of Germany, according to the official statistics of 1932. Dissimilar twins among epileptic patients were more frequent than identical twins (175 : 83). The increased incidence of dissimilar twins among epileptic patients favors polyovulation as the probable cause of twins. Conrad concludes that the mothers of epileptic patients show a tendency to polyovulation. He also notes the relatively increased incidence of dissimilar twins in the children of siblings of epileptic twins. He concludes that there is some type of correlation between polyovulation and the epileptic anlage, though he is not precise regarding the nature of the relation.

The epileptic twin was not predominantly the first-born child. In fact, in families of up to 4 siblings, the epileptic twin was usually the last child. The epileptic twin was not necessarily the first child of the pair to be born. These facts are strong arguments against the theory that birth trauma has much to do with the cause of epilepsy.

Epilepsy was found in the second twin in 3.15 per cent of dissimilar and in 6.66 per cent of identical twins. If idiopathic epilepsy alone is considered, the percentage of incidence in the second twin rises to 86 per cent for similar twins and falls to 12.5 per cent for dissimilar twins. These facts undoubtedly point to the probability that a significant hereditary factor exists in epilepsy.

There was no case of similar twins in which epilepsy was found in one twin and mental deficiency in the other. Mental deficiency occurred with four and one-half times the expected frequency among the siblings of twins. There is some correlation genetically, therefore, between mental deficiency and epilepsy, though not that of genotypic identity. With Luxenburger's method it was found that in 96 per cent of cases in which the anlage to idiopathic epilepsy existed attacks actually developed. While endogenous influences may play a rôle, hereditary predisposition is an important factor. Conrad believes that the genetic factor is important in the pathogenesis of epilepsy and that his investigation settles this controversial problem.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

DIFFUSE LEMMOBLASTOSIS OF THE CENTRAL NERVOUS SYSTEM. K. VON SÁNTHA, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:763 (Feb.) 1936.

In 1934 Foerster and Gagel reported diffuse infiltration of the brain and spinal cord with Schwann cells in a case of Recklinghausen's disease. Von Sántha reports another case in which there was no neurofibromatosis. A girl aged 9 years, who was admitted to the University Hospital in Budapest on Oct. 11, 1934, had been well until Dec. 12, 1933. On that day she fell and struck her head. She was unconscious for half an hour and vomited for three days. For about a week she complained of headache and dizziness. A gradual change in personality and character appeared after the trauma to the head. She became dull and lost interest. She began to lose weight, and precocious hirsutism appeared. A roentgenogram of the skull in April 1934 showed a parieto-occipital fracture line. Frequently recurring epileptic seizures appeared in July. Neurologic examination on July 30 gave negative results except for aphonia. Eight days after lumbar puncture left hemiplegia suddenly developed. The Wassermann reaction and the gold curve of the spinal fluid were negative. On August 20 left hemiplegia without sensory changes was found.

On admission to the hospital physical examination revealed obesity, with hypertrichosis and a blood pressure of 100 systolic and 74 diastolic. Neuropsychiatric examination revealed: hypomimia; defective blinking; slight spontaneous conjugate deviation of the eyes to the left and weakness of conjugate voluntary lateral gaze to the right; some dysphagia; left hemiplegia, including the face and the tongue on that side, with hyperreflexia and a positive Babinski sign on the left; absence of the abdominal reflexes on the left; diminution of the corneal reflexes, especially on the left, and palatoplegia, with particles of food resting on the larynx. The

patient was apathetic, somnolent and emotionally unstable. She did not speak. There were delayed responses to simple commands during the examination.

A roentgenogram of the skull showed increased digital markings, widened sutures and a moderately widened sella turcica. The temporal parts of the optic disks were atrophic; the nasal portions were edematous. Albumin and hyalin casts were present in the urine. Concentration tests of the urine gave normal results. The curve for sugar tolerance showed delay. The basal metabolic rate was minus 9.1 per cent; a urine test for pregnancy gave negative results; examination of the spinal fluid revealed: 7 cells, a total protein content of 30 mg. per hundred cubic centimeters and a sugar content of 85 mg. Epileptic attacks became increasingly frequent, and the patient died on October 29 of aspiration pneumonia.

The brain weighed 1,725 Gm.; it seemed larger and the ventricles smaller than normal. There was no change in the consistency of the brain. The corpora mamillaria, the tuber cinereum, the pons and the geniculate bodies seemed particularly large; the surface of the pons and the quadrigeminate tubercles were irregular; the hypophysis was large, and the pineal gland was normal in size. After fixation, the significant observations were: thickening of the septum pellucidum, widening of the fifth ventricle and relative thinning of the corpus callosum and anterior commissure. The cortical substance was increased, and the white matter seemed relatively diminished. The enormous size of the thalami, the geniculate bodies, the anterior quadrigeminate tubercles and the base of the pons were striking on coronal section. The medulla, the caudate nucleus, the putamen, the pallidum and the tegmentum of the pons were hardly larger than normal. The region of the cerebellar nuclei was voluminous. There was an area of softening in the right internal capsule.

Stains for myelin sheaths showed demyelinization only in the region of the dorsal nuclei of the thalamus, which was most marked caudally. The striatum profundum of the pons was poor in myelin, and the central tegmental tract was slightly pale. While the intrapontile portion of the fifth nerve was seen well on both sides, the peripheral and extrapial portions of this nerve were almost completely demyelinated. The optic tracts were involved, especially in their dorsolateral aspects.

Nissl preparations showed diffuse infiltration of the nervous system by cells with long spindle-shaped nuclei, having a distinctive chromatin structure. The neural parenchyma was spared. This infiltration was most intense in the thalamus, near the third ventricle, and in the hypothalamic region. These cells were also observed in great numbers in the tangential layers of the cerebral and cerebellar cortex. They were often seen lined up along intact myelinated nerve fibers, blood vessels and dendrites of the larger ganglion cells. They were definitely Schwann cells. Occasional mitotic divisions were noted. Satellitosis of these cells about the cell bodies of the larger ganglion cells was frequent, especially in the thalamus and the geniculate bodies. The region of the motor nuclei of the cranial nerves was relatively free from the infiltrating cells. This was also true of the anterior horn cells of the cervical portion of the cord. The marked involvement of the hypothalamic nuclei was noteworthy. The pineal gland was free from the cells. The eighth nerve, the optic tract and the fifth nerve on both sides showed diffuse neurofibromatosis. No nodules were present.

Van Gieson preparations disclosed a slight increase in the connective tissue of the leptomeninges, and hyaline changes in the walls of the small vessels in the upper layers of the cortex. The endothelium of all these blood vessels was intact. There was an increase in the fuchsinophilic connective tissue between the nerve bundles of the infiltrated eighth nerve. Bielschowsky stains showed intact axiscylinders throughout. The macroglia seemed poorly developed. No gliosis was present, and the cytoplasm and processes of some of the Schwann cells resembled those of a spongioblastoma.

Von Sántha denies any histogenic relation of the Schwann cells to the oligodendroglia. The poor development of the macroglia in this case, as well as the occasional transitional form between the Schwann cells and the macroglia cells, suggests a relation between the infiltrating lemmoblasts and the macroglia cells.

Von Sántha prefers to consider this case one of glioblastosis due to faulty development of glial elements, on the basis of a defective anlage. The trauma to the head also played a rôle. Only such a theory can explain the diffuse presence of these abnormal cells throughout the nervous system. Antoni explained the central neuroma as the result of failure to regress of elements of the neural crests which did not wander toward the spinal ganglions. Von Sántha cannot accept this hypothesis, for it does not explain the anatomic observations in his case. The probable rôle of trauma to the head cannot be overlooked in this case because of the close relation of the clinical changes to the injury of the head.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

Psychology and Psychiatry

FUNCTIONAL PSYCHOSES IN CHILDREN. L. LURIE, E. TIETZ and J. HERTZMAN, Am. J. Psychiat. **92**:1169 (March) 1936.

In a review of one thousand problem children studied at the Cincinnati Guidance Home, the authors found that twenty were psychotic. This proportion (2 per cent) suggests that mental disease is more frequent in children than has commonly been supposed. The ages of the twenty psychotic children ranged from 5 to 17 years; thirteen showed schizophrenia; one psychosis with encephalitis and six psychosis with psychopathic personality. In most of the schizophrenic group the onset was acute, whereas in all cases of psychopathic personality the development of the psychosis was insidious. In most of the children with dementia praecox intellectual impairment, taking the form of poor school work, was noted early in the illness, but actually the alteration in intelligence was not great as determined by psychometric tests. Development of antisocial trends or socially unacceptable behavior occurred at the beginning of the psychosis in most of the subjects. Eight of the thirteen schizophrenic patients came from good homes, whereas all the children with psychopathic personality had bad social backgrounds. Broken homes, for example, occurred in five of six cases of psychopathic personality and in only four of the thirteen cases of schizophrenia. The cases were reviewed many years later (on an average, six years after diagnosis); nine of the patients were in a hospital for mental diseases; three were doing fairly well in the community and three badly; one was in prison and one in a colony for the feebleminded, and three were not located. The authors believe that in the absence of organic disease or mental deficiency a child who shows a break in the normal progress of his intellectual, emotional and social development is likely to have a psychosis later in life.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

MULTIPLE INCIDENCE OF MONGOLISM IN THE SAME FAMILY. W. JOHNSON, Am. J. Psychiat. **93**:533 (Nov.) 1936.

Three cases are described. The belief that mongolism is rare in the Negro race is disputed.

JAHR, Omaha.

THE MEANING OF CHILDREN'S HABITS. SAMUEL Z. ORGEL, Arch. Pediat. **53**:463 (July) 1936.

Orgel discusses the factors responsible for the common habits of children—thumb sucking, nail biting, fidgeting, nose picking, bad dreams, night terrors, lying, stealing, enuresis, masturbation and tantrums. Psychologic or physiologic disturbances in the child are responsible for the vast majority of the problems.

Threats and punishment have an adverse influence on the habits. Leniency is the wisest course to pursue in correction. The parents should be advised that the disturbance is a nervous illness and that rigorous preventive measures and treatment by violence have no beneficial effect. Physicians and parents should take a saner view of the entire problem and be less frightened when it does occur in the young.

ORR, Buffalo.

"Accidental" Self-Injury in Children. N. W. Ackerman and L. Chidester, Arch. Pediat. **53**:711 (Nov.) 1936.

Many of the so-called accidental injuries seen in children are the result not of uncontrollable and unpredictable forces but of obscure psychologic factors. They may actually be an expression of a morbid psychic purpose. Injuries of this type are poorly understood by parents, teachers and even by some physicians.

Accidental injuries play an important part in the life of a growing child, and a tendency to such injuries is very evident in young children who are subject to temper tantrums. In older children the evidence of this tendency is more subtle and more highly disguised. A goodly number of injuries, such as cutting and mashing of fingers, stubbing toes, skinning knees and burns, must be considered as intentional and due to psychologic factors.

The purpose and indirect gain that is enjoyed by the child must be determined before solution of the problem is possible.

During the World War there were many instances of accidental injury that protected the soldiers from engaging in active combat.

To illustrate the gravity of the problem and what may be accomplished with intelligent interpretation and guidance the authors present their interesting experiences with a 12 year old girl who suffered from serious social maladjustment, educational retardation, a habit of lying, sexual misdemeanors and a badly scarred left hand and arm. It was observed that she suffered minor accidental injuries each and every day. The injury always occurred where it could be prominently seen. Following an injury she became sullen and charged those about her with responsibility for the accident. At first sympathy was bestowed on her. However, it was noticed that the patient took many unnecessary risks and invited accidents. Sympathy and attention were withdrawn, and her condition became worse. Gradually she was convinced that the purpose of the therapy was to help her and not to accuse and punish her. Gradually she told more of her storm-tossed life, and under proper guidance she gradually modified her sadistic, masochistic and antisocial tendencies until she became completely adjusted to her environment and developed into a normal child.

Orr, Buffalo.

Mental Retardation and Juvenile Delinquency. Eleanor Glueck, Ment. Hyg. **19**:549 (Oct.) 1935.

The relationship between feeblemindedness and delinquency cannot be determined simply by correlating these isolated factors. It is essential to correlate many other sociologic and cultural factors with intelligence. In order to do this, Glueck analyzed the histories of one thousand juvenile delinquents who had been referred to the Judge Baker Foundation. She found that 13 per cent of the delinquent children were mentally defective, whereas only 1.5 per cent of school children from the same areas were so. This disproportion does not arise from the fact that the retarded delinquent child is more easily caught and convicted than his brighter confederate, as shown by the similarity of the figures for recidivism and the age at arrest for the intelligent and the retarded groups. In order to make a more detailed analysis, Glueck divided the group into two divisions, a normal section (intelligence quotient over 80) and an inferior section (intelligence quotient under 80). Thirty-eight per cent of the subjects fell into the second group. The influence of heredity seemed material, since mental defect was found in the families of 45 per cent of the normal and 73 per cent of the inferior group. In the subnormal group the mothers were usually younger than those in the group of normally intelligent children. Of the parents of the normal group 24 per cent were illiterate, while 41 per cent of the parents of the retarded subjects were unable to read.

The families of the group with inferior intelligence were, on the whole, more indigent than those of the other group, as 85 per cent of the former and only 73 per cent of the latter were on the "ragged edge of poverty." On the other hand, a greater proportion of the group with normal intelligence were before the court for crimes involving property, while the relative positions were reversed for

other offenses. At the end of the period of "treatment" in the court and clinic, 90 per cent of the group with the lower intelligence continued to be delinquent, as compared with 84 per cent of the subjects with normal intelligence.

Glueck concludes that there are more feebleminded persons in delinquent groups than in the general population, that mental deficiency, though not a direct cause, is a potent contributing factor and that such differences of behavior as exist between normal and retarded delinquent children arise from the mental deficiency. A knowledge of this should inspire teachers of classes of retarded children to recognize their greater responsibility to the community and should result in more intelligent special training of such children.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

THE SLEEP OF YOUNG CHILDREN IN A TWENTY-FOUR HOUR NURSERY SCHOOL. MARTHA REYNOLDS, Ment. Hyg. **19**:602 (Oct.) 1935.

A study of the sleep of nursery school children at the Vassar College summer school indicates that children between the ages of 2 and 3 years sleep approximately twelve hours and a half daily; those between the ages of 3 and 4 years, eleven and a half hours, and those between the ages of 4 and 5 years, eleven hours. Other factors, such as physical condition and emotional stability, probably affect the amount of sleep required. Reynolds asks whether the old standards were not too high and therefore the cause of anxiety and tension over the sleep problem. Children of all groups in the nursery school took approximately one hour instead of twenty minutes to go to sleep at night, and at nap time, half an hour.

It is suggested that specialists give serious consideration to the standards of sleep they urge parents to follow, since a revision of the attitude toward sleep similar to that of the attitude toward eating may be necessary in order to avoid the manufacture of sleep problems. Although the variations in the amount of sleep taken by individual children from day to day were large and inconsistent, the small variations in the weekly, biweekly and triweekly averages seem to indicate that, for a week or a longer period, there may be a tendency to maintain a fairly constant balance of sleep. Reynolds suggests that, instead of overemphasizing the importance of immediate external conditions, one should establish regularity of hours for rest, provide conditions conducive to sleep and arrange an adequately balanced day, free from emotional strain. If this is done, the physiologic demand for rest can be trusted to provide adequate and more or less automatic regulation.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

A STUDY OF FOUR HUNDRED JUVENILE DELINQUENTS. W. B. OSGOOD and C. E. TRAPP, New England J. Med. **215**:623 (Oct. 1) 1936.

Of the 400 delinquent young persons studied, 328 were boys and 72 were girls. Their ages varied from 8 to 18 years. The greatest number of delinquents who are brought before the court appear to be between the ages of 14 and 16 years.

The chief offenses of the girls were sexual; they tended to occur after the onset of puberty. Among the boys, larceny was the most frequent offense. Unlawful use or larceny of an automobile was represented in 147 offenses.

The average intelligence quotient (Binet-Simon) of the delinquent youths studied indicated a borderline intelligence rating; 21 per cent of the boys and 29 per cent of the girls were feeble-minded. Psychiatric studies revealed that 8 delinquents were definitely psychotic; 14 were classified as psychopathic personalities, and 2 were epileptic. Four boys carried weapons, and the most serious offense was that of arson.

A study of the quality of the home in relation to the number of offenses committed shows no correlation, as there are the same number of offenses in good and bad homes.

GENGENBACH, Denver.

CONGENITAL ARITHMETIC DISABILITY AND ACALCULIA (HENSCHEN). ERICH GUTTMANN, Brit. J. M. Psychol. **16**:16, 1936.

Guttmann believes that isolated arithmetic disability is rare. In fact, it has been maintained by some authors that mathematical skill is not a specific ability. Henschen, however, has distinguished an acalculia which is distinct from number alexia or agraphia. Idiokinetic (distorting) and constructional (confusing of position) types of agraphia have been described, and Guttmann illustrates the relation of the constructional type to difficulties in calculating. He points out that in illiterate persons calculating is independent of figure writing. He found that eleven of fifteen children with difficulty in reading were normal in arithmetic. The possible relations to the visual system and to the "parietal syndrome" are discussed. Guttmann concludes that the few cases he reports "point to the interrelations being diverse." He is inclined to believe in a causal focal anomaly of the brain, which, however, does not preclude training in simple calculation by methods more circuitous than those used in the normal person. The functions found to be intact determine the method in the individual case.

ALLEN, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

THE STRAIN OF SCHOOL LIFE ON GIRLS DURING THE EARLY MENSTRUAL PERIOD. D. J. GAIR JOHNSTON, Brit. M. J. **2**:892 (Nov. 9) 1935.

This study is a condensed account of an inquiry carried out at the request of an authority on education to determine the effect of the strain of school life on the physical welfare of girls during the somewhat critical period of the early menstrual years. The physical development of girls between the twelfth and the fifteenth year is much more rapid than that of boys. In this period sexual development, with all its attendant disturbances, is active. Girls are more conscientious; hence, this rapid physical and sexual growth coincides with a strenuous educational effort. Their standard of fitness is less than that of boys and depreciated more during the period of this study. The investigation showed conclusively that home work required a greater expenditure of energy by girls and, therefore, greater care ought to be exercised in guarding their health.

BECK, Buffalo. [ARCH. NEUROL. & PSYCHIAT.]

TREATMENT WITH ACETYLCHOLINE FOR CERTAIN CHARACTER CHANGES IN CHILDREN WITH A TENDENCY TO IMPULSIVE BEHAVIOR. J. DUBLINEAU and DORÉMIEUX, Ann. méd.-psychol. **94**:99 (June) 1936.

Several authors have observed a favorable effect from the use of acetylcholine in epilepsy. The frequency of the seizures decreases, and in some instances there is improvement in the epileptic disturbance. This induced Dublineau and Doremieux to use acetylcholine in the treatment of delinquent children with personality changes characterized especially by impulsive behavior—temper tantrums, violence and chronic disobedience. They report four cases in which daily injection of from 50 to 100 mg. of acetylcholine associated with administration of phenobarbital by mouth was followed by definite improvement in behavior, with diminution or disappearance of the impulsive tendency. The improvement was noted soon after the beginning of the treatment. It was temporary, however, was effective only during treatment and rarely lasted more than a few weeks. The treatment had no untoward effects and was well tolerated.

YAKOVLEV, Waltham, Mass. [ARCH. NEUROL. & PSYCHIAT.]

SPEECH DEFECT IN ABNORMAL CHILDREN. M. WAHL, Gaz. d. hôp. **109**:1513 (Nov. 4) 1936.

Wahl reports six cases, in five of which other neurologic signs were present, indicating an organic lesion. In the sixth case repeated convulsions were a feature. Although all the patients had low intelligence quotients, retardation of the speech was much more pronounced than the general mental retardation. It was impossible to analyze these aphasias further.

KAJDI, Baltimore.

PSYCHOLOGIC INSPECTION: THE NEED FOR IT AND ITS AIMS. V. KOVARSKY, Rev. méd.-sociale de l'enf. **4**:389 (Nov.-Dec.) 1936.

The report is a summary of the program which has been evolved during the past eight years for the psychologic inspection of school children in Montpellier, and Mlle. Kovarsky throughout stresses the need for close cooperation between the family, the school teachers, the doctors and the psychologists. It is emphasized that the psychologic examination is not substituted for the medical, psychiatric and usual academic examinations but the knowledge obtained is used to supplement the information from the latter. Backwardness in children is viewed as an end-result of social and hygienic as well as organic factors; therapy is directed as indicated by the underlying condition. The author wisely points out that the demands on a backward child should be adjusted to his capacity instead of attempting to make him fit a fixed environment. DIETRICH, Los Angeles.

SCHIZOPHRENIA IN A BOY FOUR YEARS OLD. S. Z. GALATSKAYA, Sovet. psikhonevrol., 1936, no. 2, p. 117.

This case is one of a series which have been reported from the Children's Psychiatric Clinic of Tatiana Simson, Moscow. Simson is convinced that schizophrenia can develop at the age of 2 or 2½ years. A boy aged 4 years and 3 months entered the children's psychiatric clinic because for a year he had been nervous, jumpy, antagonistic, stubborn and aggressive. Up to the age of 2½ years, he had been happy, quiet and cheerful. He liked to play with toys and was good in games involving manual dexterity. He did not play with children but, on the other hand, did not avoid them. There were no fears. He was musical and began to reproduce various tunes at the age of 1½ years. At about the age of 3 there was a marked change. He became withdrawn, overactive, confused in behavior, irritable and unable to concentrate on any task. He began to talk to himself; stammering developed and was interpreted as an attempt of the child to imitate his father, who was a stammerer. He refused to stay in his room and insisted on being in the company of adults. For no apparent reason, he began to attack children and adults. At the same time, he was unable to defend himself. His memory was excellent, and his intellectual development was progressing without delay.

When the child was admitted to the psychiatric clinic, it was noticed that he was irritable, overactive, extremely hostile and aggressive. There was much diffuse, meaningless activity. He attacked other children a great deal, for no reason. Speech was fragmentary, disconnected and rather incoherent. Neurologic examination gave negative results. The intellectual functions were intact. It was the impression of the psychiatrist that the child was living in an autistic world, with beginning disturbance of associative thinking, evidenced by choppy, disconnected productions. The boy was observed in the clinic for only three weeks. In commenting on the case, Galatskaya states that the boy's defenselessness and his complete inability to adjust himself to a new environment in spite of good intellect show that he had lost his sense of reality. The emotional factors in the case are not discussed. KASANIN, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Genito-Urinary Tract

EFFECT OF DIETARY PROTEIN ON THE UREA CLEARANCE OF CHILDREN WITH NEPHROSIS. L. E. FARR, J. Clin. Investigation **15**:703 (Nov.) 1936.

In four children with the nephrotic syndrome, all aged 4 years, the urea clearance was found to vary markedly with the intake of protein. Protein intakes of 0.5, 1, 2, 3 and 4 Gm. per kilogram per day were accompanied by average urea clearances of 73, 88, 178, 184 and 216 per cent of mean normal, respectively. The effects of these protein intakes on the urea clearance in the 4 year old patients were much greater than similar effects observed in adult human subjects, either normal or with renal disease. GUEST, Cincinnati.

RUPTURED OVARIAN CYST IN CHILDHOOD. G. C. KING and C. H. HAWES, New England J. Med. **215**:576 (Sept. 24) 1936.

A ruptured ovarian cyst in childhood is an uncommon lesion. A girl aged 12, a student, was admitted to the Truesdale Hospital, complaining of severe pain in the right lower quadrant of the abdomen of two hours' duration. Three weeks previously, while at school, she had had her first attack of this kind. It was so severe that she could not walk and had to be carried home. She quickly recovered from this attack, however, and was up and about the following day. The day prior to the second attack she felt well, danced in the evening and slept all night. The following morning about 7:30 she got out of bed as usual and began to dress for school. She was seized with an intense pain in the right lower quadrant which made her cry out and double up. She was unable to move and had to be carried to bed. The temperature was 99 F. by mouth; the pulse rate was 140, and the respiratory rate, 22. The skin and mucous membranes were extremely pale. There was generalized tenderness below the umbilicus.

About four hours after the onset of the attack the patient was taken to the operating room. The abdominal cavity was full of bright red fluid which gushed forth as soon as the peritoneum was opened. On the right were found the frayed edges of a cystic ovary which had ruptured, there apparently being no normal ovary left.

The diagnosis was: follicular cyst of the ovary, ruptured.

GENGENBACH, Denver.

TERATOMA OF THE OVARY AND THE INFLUENCE OF THE ENDOCRINE GLANDS ON TUMORS OF THE OVARY IN CHILDHOOD. J. R. DREYFUS, Arch. de méd. d. enf. **39**:721 (Nov.) 1936.

The early diagnosis of a malignant tumor, even a cancer, may result in complete and permanent relief. Dreyfus reports an observation in a girl under 3 years of age who sustained a slight injury which provoked a torsion of the pedicle of a tumor of the left ovary. Operation revealed a cancer of this organ, and its removal has been followed by normal health for the past six years.

Two further cases are reported in this contribution. The first concerned a girl of 12 who suffered occasional attacks of menorrhagia with abdominal cramps; the child had the appearance of a mature female. Examination revealed a tumor in the hypogastric region, as large as a coconut, and operation disclosed a solid teratoma of the left ovary, with torsion of the pedicle. In spite of radiotherapy, metastases promptly supervened, and the patient succumbed.

In the second case, a girl of 5 had complained frequently of abdominal pains, but examination was delayed until a tumor of sufficient size to reach the left hypochondrium had developed. A laparotomy showed the right ovary involved in the tumor, which weighed 1,500 Gm., and histologic study demonstrated that this neoplasm was an embryonal teratoma of unquestionably malignant tendencies. The child died five days afterward, from shock and hemorrhage.

AMESSE, Denver.

CARCINOMA OF THE OVARY IN A GIRL TWELVE YEARS OF AGE. H. DE SA, Bull. Soc. d'obst. et de gynéc. **25**:507 (July) 1936.

The patient was an unmarried Hindu girl 12 years old. She had never menstruated, showed no signs of puberty and was greatly emaciated. Rapid enlargement of the abdomen had been noted for two months. The tumor filled the pelvis, rising to a point 2 fingerbreadths below the umbilicus. It had a firm irregular surface. The preoperative diagnosis was sarcoma of the uterus. At operation a large vascular mass, which bled easily, was found involving all the internal genital organs. These were removed in toto. There was considerable hemorrhage, and the child died fifty-four hours after operation. The pathologic diagnosis was carcinoma of the ovary. The article is well illustrated, and a detailed report of the necropsy is given.

GLASER, Rochester, N. Y.

Treatment of Vulvovaginitis of Gonococcic Origin in Infants. S. Graçoski, E. Hurmuzache, Alexenco and Weissbuch, Bull. Soc. de pédiat. de Iasi **7**:5 (Jan.-March) 1936.

Nineteen infants with gonococcic vaginitis which was resistant to ordinary forms of treatment were treated by intravenous injection of the stock vaccine (Dr. I. Cantacuzino). The first doses were very small, from 0.01 to 0.02 cc., and were increased gradually to from 0.7 to 0.8 cc. Forty-two per cent were cured with from ten to fifteen injections (from thirty to thirty-five days) and the others with from twenty to thirty injections (from fifty to sixty days).

Leslie, Evanston, Ill.

The Humoral Syndrome During the Long Course of Acute Hemorrhagic Nephritis in a Girl Nine Years Old. Nobécourt, Veslot, Briskas and Navarron, Bull. Soc. de pédiat. de Paris **33**:398 (June) 1935.

A girl 9 years old was admitted to the hospital with acute hemorrhagic nephritis, which had developed insidiously, presumably after a pharyngeal infection. The tonsils had been removed a year previously. During the course of the disease the blood showed a high nitrogen, a low albumin and a high globulin content, an increase in the amount of lipids and hypercholesteremia. These values gradually returned to normal during four months; the urine still showed traces of albumin. Because of a long coagulation time as well as a positive reaction to the capillary resistance test, the possible etiologic significance of avitaminosis C is mentioned.

Benjamin, Montreal, Canada.

A Case of Renal Sporotrichosis. Jules Milhit, André Martin and Jeanne Delon, Bull. Soc. de pédiat. de Paris **33**:592 (Dec.) 1935.

A boy 19 months old had an enlarged right kidney, which was removed and found to contain a large amount of pus. Histologic examination showed necrotic lesions, with surrounding inflammatory reaction, and more numerous larger lesions formed of concentric alternate layers of acidophilic necrotic material and of pus. In the layers containing the former substance examination with an oil immersion lens revealed refractile bodies and a few pyriform elements which resembled the spores of sporotrichosis. No culture of the pus was made, and no agglutination test was done.

Benjamin, Montreal, Canada.

Urinary Lithiasis in Infancy. R. Ercole, An. de cir. **2**:3 (May) 1936.

Swift Joly, of San Peter's Hospital, London, observed 10 patients under 20 years of age among 197 patients with urinary lithiasis. Hager, of the Mayo Clinic, found 22 children among 2,621 persons with urinary lithiasis. Bugbee and Wollstein in a series of 5,000 autopsies in infants under 1 year found 13 cases of calculi in the kidneys, all accompanied by infection. In Russia, India and China there has been reported a high incidence of urinary lithiasis in children. In China J. O. Thomson, of the Hospital of Canton, observed 3,890 cases in children under 15 years; Assendelft observed that of 630 cases in Russia, 77 per cent were in children under 10 years of age; and Civiali in 1880 noted that, of 5,900 cases of urinary lithiasis, 45 per cent were in children.

Ercole does not find so high an incidence. Of 60 cases reported by various Spanish authors, 8 per cent were in children. There is no predilection for sex. The majority of the calculi are formed of uric acid crystals or urates, of calcium oxalate or of the triple phosphates. Calcium oxalate and ammonia urates formed the nuclei in the majority of the cases. These two substances are in relation to uric acid in the proportion of 4:1. The presence of triple phosphates indicates the changes due to infection as a result of the action of the calculi. The majority, about 70 per cent, of the calculi are found in the bladder.

The symptoms include colicky pain, vomiting and gastro-intestinal upsets, which frequently complicate the picture so that lithiasis is not thought of until much

later, when frank hematuria occurs. It is frequently overlooked and the diagnosis of chronic pyelitis made. It must be differentiated from retrocecal appendicitis, in which hematuria may be present. Now that urography is so easy, it is an important help in making the diagnosis.

The treatment is medical and surgical. The medical treatment includes symptomatic relief and a dietary regimen. In most cases surgical measures are resorted to. Ercole believes that a kidney that functions poorly is better than no kidney. He reports five cases.

HERRON, Spokane, Wash.

TREATMENT OF PYURIA IN CHILDREN. E. UNSHELM, Arch. f. Kinderh. **109**:65, 1936.

A derivative of sulfanilamide, prontosil soluble (the disodium salt of 4'-sulfamidophenyl-2-azo-7-acetylamino-2-hydroxynaphthalene-3, 6-disulfonic acid), was employed in thirty-four cases of pyuria in children with excellent results. In thirty-two of these cases Bacillus coli was cultured from the urine before treatment. It is important that the therapy should not be discontinued too soon, as relapses may occur. Fourteen days of treatment is usually sufficient. No side reactions were observed with older children except in two to whom unusually large doses (20 cc.) were given intramuscularly. In infants, however, vomiting or diarrhea occasionally necessitated reduction in the size of the dose or parenteral administration.

CRANE, Washington, D. C.

CRYPTORCHIDISM: II. END-RESULTS OF OPERATION, WITH SPECIAL REFERENCE TO THE ABILITY TO PROCREATE. J. SCHULZ, Deutsche Ztschr. f. Chir. **247**: 357 (July 30) 1936.

A study of the end-results of operation for unilateral and bilateral undescended testes gives the impression that when the operation is done at the proper time (between the ages of 9 and 10 years) the growth of the hypoplastic testis is stimulated and its otherwise unavoidable atrophy prevented. Even with bilateral undescended testes it is nearly always possible to avoid hypogonadism. Patients successfully operated on show no abnormality of physical or physiologic development. When possible the procedure of Mauclaire *(synorchidie)* was followed with bilateral undescended testes. The principle of this operation is the sewing together of the two testes in the sac at the scrotal septum. In most instances patients successfully operated on had children following marriage.

GLASER, Rochester, N. Y.

METABOLISM OF CREATINE IN PUBERTAS PRAECOX. I. SCHARFF, Monatschr. f. Kinderh. **67**:273 (Nov.) 1936.

Scharff reports a case confirming her previous observations. A 5 year old girl had been menstruating regularly for a year. Creatine, given both parenterally and enterally, was excreted quantitatively. This reaction is typical of all children before puberty. The premature sexual maturity had no influence.

GERSTLEY, Chicago.

ROENTGEN TREATMENT OF DISTURBANCES OF MENSTRUATION IN YOUNG WOMEN. J. B. PORCHOWNIK and W. W. WITTENBURG, Röntgenpraxis **8**:695 (Oct.) 1936.

Those aspects of this paper which relate to the effect on the fetus of roentgen irradiation of the mother before conception may interest the pediatrician. Neither the authors' own experience nor a review of the literature provided them with any reason to believe that children conceived and born after roentgen irradiation of the mother are injured thereby.

MCCUNE, New York.

A Report on the Catamenia of Two Thousand Chinese School Girls. S. W. Chang, Chinese M. J. **50**:973 (July) 1936.

This report comes from the Changsha Union Hospital, in Hunan, China. Among the Chinese school girls examined, mostly Hunanese, the most frequent age at which menstruation is established is 14. About 9 per cent began to menstruate at 12 years, 27 per cent at 13 and 20 per cent at 15. Chang has figures also on the interval and duration, the most frequent being 30 and 3 days, respectively. There were nine cases of nosebleed and three of bleeding of the gums coincidental with the uterine bleeding.

Neff, Kansas City, Mo.

Relation Between the Formation of Renal and Vesical Calculi and Nutrition. A. Polak, Nederl. tijdschr. v. geneesk. **80**:5648 (Dec. 19) 1936.

Polak succeeded in producing renal and vesical calculi in about 100 per cent of young white rats that were on a full diet by adding calcium carbonate to the food in the proportion of 3 per cent. In old white rats, young white mice and guinea-pigs no calculi were formed. Administration of potassium dihydrogen phosphate in the same proportion instead of calcium carbonate did not produce stones, nor did addition of calcium chloride in the same proportion. It appeared further than a 2 per cent addition of calcium carbonate also produced stones, but a 1 per cent addition did so only exceptionally. Equivalent quantities of calcium lactate also produced stones but to a much less extent. Finally it was shown that administration of sodium bicarbonate, calcium gluconate and calcium phosphate together with calcium carbonate did not yield stone formation.

van Creveld, Amsterdam, Netherlands.

Changes and Formation of Calculi in the Urinary Passages of White Rats Kept on Diets Rich in Calcium. P. Arons and M. P. J. van der Rijst, Nederl. tijdschr. v. geneesk. **80**:5652 (Dec. 10) 1936.

This is a description of the alterations found in the kidneys and urinary passages of young white rats kept on a diet rich in calcium. These alterations are characterized by proliferation of epithelial cells and connective tissue and, in the ureter and bladder, also of the muscular coats to such an extent that the lumens of the passages are lined by an epithelium of several layers and a multicellular argentophil connective tissue, which makes the lining bulge locally by proliferation. To this is added intense infiltration by wandering cells, making an impression of infection. These wandering cells also migrate into the lumens and contribute to a great extent to the organic framework of the calculus. Bacterial stains gave a negative result.

van Creveld, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

Pituitary Growth Factor. E. K. Shelton, California & West. Med. **45**:20 (July) 1936.

Shelton reviews the literature dealing with extracts from the anterior lobe of the pituitary gland and records his own experiences with their clinical use. Sample histories are presented. He concludes that during the growth period, growth can be stimulated. Dwarfism in which the growth increment is 50 per cent or more deficient, cannot be prevented, but in persons who are from 25 to 50 per cent deficient in growth increment the extracts now available are potent enough to maintain growth at or slightly above the normal rate. Indiscriminate use of the extract should be discouraged because of the possibility of contamination with other pituitary fractions, producing antagonistic influences. The study is being continued, and more observations are necessary before definite conclusions can be arrived at.

Marshall, San Francisco.

THE BLOOD LIPIDS OF DIABETIC CHILDREN. I. L. CHAIKOFF, F. S. SMYTH and G. E. GIBBS, J. Clin. Investigation **15**:627 (Nov.) 1936.

Lipid constituents (total lipids, free and esterified cholesterol, phospholipids and fatty acids) were determined in the whole blood of twenty-six diabetic and twenty-three nondiabetic children. The results of the study showed that, with control by insulin and diet, diabetic children have blood lipid values well within the normal range.

GUEST, Cincinnati.

THE GLYCEMIC RESPONSE TO ISOGLYCOGENIC QUANTITIES OF PROTEIN AND CARBOHYDRATE. J. W. CONN and L. H. NEWBURGH, J. Clin. Investigation **15**:665 (Nov.) 1936.

In normal and diabetic subjects a comparison was made between the glycemic and glycosuric responses after ingestion of equivalent amounts of dextrose derived from dextrose, protein (lean beef) and carbohydrate foods (potato, bread, banana). These studies indicate a decided advantage to the diabetic person of deriving dextrose from protein, owing to the slow rate of liberation of dextrose into the blood stream during metabolism of protein.

GUEST, Cincinnati.

SALT AND WATER METABOLISM OF ADRENAL INSUFFICIENCY AND PARTIAL STARVATION IN RATS. M. I. RUBIN and E. T. KRICK, J. Clin. Investigation **15**:685 (Nov.) 1936.

Studies of balance were made for water, sodium, potassium, calcium, magnesium, chlorine, phosphorus and nitrogen on rats before and after adrenalectomy, with and without salt therapy, and in normal rats during partial starvation. Adrenal insufficiency was associated with losses from the body of all the elements investigated, and in partial starvation the negative salt balances were similar but of lesser magnitude. It was suggested that the adrenal gland influences the general electrolyte and water balances, not specifically the sodium or potassium balances. Salt treatment was of value but did not completely restore the adrenalectomized rat.

GUEST, Cincinnati.

BLASTOMA OF THE ADRENAL. W. LE FEVRE, J. Michigan M. Soc. **35**:94 (Feb.) 1936.

A 4 year old boy presented abdominal distention, pain in the legs, secondary anemia and continued elevation of the temperature. Agglutination tests with Brucella abortus and Brucella melitensis were positive. The diagnosis of blastoma of the adrenal was made following autopsy.

CAREY, Detroit.

THE RÔLE OF THE THYMUS AND PINEAL GLANDS IN GROWTH AND DEVELOPMENT. L. G. ROWNTREE, J. H. CLARK, A. STEINBERG, N. H. EINHORN and A. N. HANSON, New York State J. Med. **36**:1277 (Sept. 15) 1936.

Daily intraperitoneal injections of 1 cc. of thymus extract were given to successive generations of rats. These rats showed striking gains in weight and growth up to the seventh generation and acceleration in the processes of development up to the tenth generation. Their teeth erupted earlier and showed an increased rate of growth. The medullation in the spinal cord showed marked increase. The difficulties of standardizing and preserving thymus extracts are stated. Thymic implants give much the same results as injected thymus extracts.

Thymectomy in successive generations is followed by definite retardation in weight and slight retardation in the rate of development.

Roentgen radiation was given in moderate doses to new-born rats in two successive generations. A retardation of growth was shown. A study of the effects of the treatment with radiation is not yet complete. It is difficult to limit the exposures to the thymus, avoiding other tissues.

Pineal extract injected into successive generations of rats retarded growth but accelerated the rate of development.

AIKMAN, Rochester, N. Y.

ENDOCRINE STUDY OF HYPOGONADISM AND CRYPTORCHIDISM. M. B. GORDON, New York State J. Med. **36**:1313 (Sept. 15) 1936.

Every child with hypogonadism or cryptorchidism should be studied from the point of view of endocrinology. Cryptorchidism may be due to deficiency of the pituitary, thyroid or testicular gland. Gordon gives thyroid extract and the gonadotropic hormone from the urine of pregnant women by mouth in increasing doses. Hypodermic injections of anterior pituitary are added in some cases. In a third group the gonadotropic substance from the urine of pregnant women is added. The best results are obtained in the last group.

AIKMAN, Rochester, N. Y.

SYMPOSIUM: ENDOCRINE GLANDS. H. R. GEYELIN, New York State J. Med. **36**: 1600 (Nov. 1) 1936.

This symposium was presented at a state meeting dealing with diabetes, ovarian therapy and tumors in and around the pituitary gland.

AIKMAN, Rochester, N. Y.

THE HISTOPHYSIOLOGIC MECHANISMS OF THE HYPOPHYSIS. A. POLICARD, Arch. de méd. d. enf. **39**:393 (July) 1936.

Clinical, biochemical and physiologic research of the past few years has added so prodigiously to knowledge of the hypophysis that it not only has taken its deserved position among the ductless glands but also is recognized as an agency for fundamental control of the entire economy.

Notwithstanding these advances in the conception of its functions and its remote influences, the mechanisms utilized by the pituitary gland in the achievement of these objectives are still shrouded in profound obscurity. On section of the gland, one is immediately impressed with the extraordinary complexity of its structure—masses of cells apparently scattered in great disorder through a complex melange of connective tissue, showers of nuclei, colloid vesicles, etc. From this confused group of histologic elements, however, are developed the powerful hormones physicians are now beginning to recognize and to classify. How do these cell masses function? What bonds, what affinities unite them? How do they secrete? Numerous problems such as these at once present themselves. In spite of twenty years of intensive study, the histophysiologic relations of this structure have only in small part been revealed; few indeed of the endocrine organs have so successfully concealed their intimate functions.

In discussing the general histologic aspect of the hypophysis and the recognition of its double embryologic origin, one should keep in mind that this duality does not imply independence but rather a conjoint action, especially as it relates to vascular organization, to the zone of contact between the lobes and to the disposition of certain products of secretion.

An exhaustive review of the minute anatomy of the anterior lobe and its constituent elements follows. The characteristics of the chromophobic cells, the acidophilic and basophilic granulation cells and the cells appearing during pregnancy are described, and their possible relationship is outlined.

The study extends to the posterior and the intermediate lobe, with a review of the recent literature.

AMESSE, Denver.

THE HYPOPHYSIS AND THE PREPUBERTAL PERIOD. G. MOURIQUAND, Arch. de méd. d. enf. **39**:407 (July) 1936.

Two phases are distinguished in the growth and development of youth, the first characterized by an increase of stature and possibly of weight, which may be considered as the prepuberal period, with its beginning at about 11 years for girls and 12 years for boys. The second period, which immediately follows the first, is that of real puberty and is marked by the development of both primary

and secondary sex characters. Such a division is important, Mouriquand asserts, from both a biologic and a medical point of view; its psychologic and educational aspects are likewise vital. In this connection, it must be recognized that there are many factors—hereditary, congenital or acquired—which may impede or wholly obstruct this normal cycle.

Biologists agree that animal organisms are composed essentially of the somatic portion, from which is derived the body itself, which is ephemeral and doomed to die. This segment must be compared with the germ plasm, the source of sexuality, the genital organs, reproduction and the continuity of the species; it may therefore be regarded in a sense as immortal. Whatever may be the value of such a conception and of such an arbitrary separation of soma and germ plasm, it is most convenient in differentiating prepuberty from puberty, when the stimulating factors of growth of the body may be contrasted with those of sexual development.

After birth and up to late childhood the activity of the thymus gland, the secretions of which are poorly understood, seems to possess a dominating rôle in corporeal growth, but with the onset of puberty the functions of the thymus are transferred to other glands in the endocrine system, especially the thyroid and the hypophysis in close alliance with the parathyroids and the adrenals. The hormone of the pituitary gland in the prepuberal years must be considered, however, as the activating agent in normal growth, which is paralleled by corresponding increase in weight.

In his exhaustive thesis Mouriquand develops further the present day point of view concerning the successive changes incident to preparation of the organism for puberty.

AMESSE, Denver.

THE TECHNIC OF HYPOPHYSIAL THERAPY IN CHILDREN. P. LEREBOULLET, Arch. de méd. d. enf. **39**:442 (July) 1936.

Progress made in knowledge of the physiology of the pituitary gland and of the functions of the anterior and the posterior lobe together with those of the pars intermedia justifies one in the hope that there may soon be isolated therapeutic principles comparable in action to those separated from the thyroid gland and the adrenal glands.

It has already been established that, unlike the administration of thyroid extract, hypophysial therapy administered by the buccal route is not followed by results comparable to those obtained through subcutaneous injection; it is likewise generally recognized that injections of the total extract are relatively inactive. To secure a satisfactory response, glandular therapy in this instance must be dissociated. The use of the extract of the posterior lobe has been a common procedure for more than twenty years, while the value of the anterior lobe is becoming more and more appreciated. Zondek has demonstrated the presence of a special hormone in the pars intermedia.

In the management of certain disorders it may become necessary to employ other glandular extracts in conjunction with those of the hypophysis, and it is in these cases that keen discernment is essential to avoid illogical and unscientific therapy.

The indication and the dosage in various diseases of childhood are discussed in full.

AMESSE, Denver.

THERAPY FOR TUMOR OF THE HYPOPHYSIS. PIERRE PUECH and LOUIS STUHL, Arch. de méd. d. enf. **39**:461 (July) 1936.

Two methods of treatment for tumor of the hypophysis are now being used, neurosurgical intervention and roentgenotherapy. The type of management in a given case will be determined not only by the nature of the tumor but also by its stage of evolution at the time of examination. The importance of early and exact diagnosis is apparent.

While relatively easy, diagnosis is usually made late in spite of the advance in technic.

The most common tumor of this gland is the adenoma, which is further differentiated into three types, the chromophobic, the acidophilic and the basophilic. Next in frequency is the craniopharyngioma, which is congenital. All the forms are carefully described, and indications for treatment are outlined.

AMESSE, Denver.

CURE OF THYMIC HYPERTROPHY IN A CHILD NINETEEN MONTHS OF AGE BY ROENTGEN RAYS. E. HURMUZACHE and S. PINELES, Bull. Soc. de pédiat. de Iasi **6**:75 (Oct.-Dec.) 1935.

The child suffered from difficult respiration and frequent attacks of cyanosis. The roentgenogram showed an enlarged thymus, and there was disappearance of the symptoms following two roentgen treatments. LESLIE, Evanston, Ill.

OBSERVATION OF A NEW SYNDROME (BIEMOND) RESEMBLING THE LAURENCE-MOON-BARDET SYNDROME. A. DELHAYE and L. VAN BOGAERT, J. belge de neurol. et de psychiat. **36**:420 (July) 1936.

Biemond described a familial condition consisting essentially of infantilism of the hyopituitary type, coloboma of the iris, polydactyly, skeletal anomalies and mental retardation. He compared this symptom complex with the familial Laurence-Moon-Bardet syndrome. At autopsy Biemond observed a small pituitary gland, hydrocephalus with hydromyelia, a cerebral tumor and intestinal polyposis with carcinomatous degeneration of several of the tumors. Delhaye and van Bogaert report a similar case in which they made complete studies. The clinical characteristics were: obesity of the hypophysial type, with abnormal development of the skeleton, symmetrical brachydactyly, kyphosis, bilateral atypical coloboma genital hypoplasia, marked mental retardation, abnormalities in water and lipoid metabolism, eosinophilia, and a lowered basal metabolic rate. Four members of the family also showed some of these changes. The authors believe that this symptom complex can be differentiated from the Laurence-Moon-Bardet syndrome.

WAGGONER, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

STIMULATION OF MAMMARY SECRETION IN DOGS BY ANTERIOR PITUITARY EXTRACT. B. A. HOUSSAY, Rev. Soc. argent. de biol. **11**:240 (July) 1935.

Injection of anterior pituitary extract produced an increase in secretion in the breasts of dogs when the breasts were sufficiently developed. The factors influencing the results were numerous. The most important was the degree of development of the breasts.

If there was an adult pendulant breast, the increase in secretion was easily obtained. In the poorly developed breast of the juvenile or infantile type, no secretion was obtained. In pregnant dogs and dogs in the postpartum stage no results were obtained, nor in normal males, castrates, thyroidectomized dogs, hypophysectomized and castrated dogs or dogs with the splanchnic and lumbar sympathetic nerves resected.

The activity of the extract was destroyed in fifteen minutes at 100 F., but not in fifteen minutes at 70 F. HERRON, Spokane, Wash.

PRODUCTION OF MAMMARY SECRETION IN MALE GUINEA-PIGS BY ANTERIOR PITUITARY EXTRACT. J. L. SARDI, Rev. Soc. argent. de biol. **11**:250 (July) 1935.

Injection of anterior pituitary extract did not produce secretion in the breasts of male guinea-pigs. But if the male guinea-pigs were first given injections of an estrogenic substance, the breasts became hypertrophied, and then injection of anterior pituitary extract produced secretion of milk.

HERRON, Spokane, Wash.

DIABETOGENIC ACTION OF THE ANTERIOR PITUITARY INDEPENDENT OF THE ADRENALS. B. A. HOUSSAY and L. F. LELOIR, Rev. Soc. argent. de biol. **11:** 464 (July) 1935.

The diabetogenic action of the extract of the principal lobe of the pituitary gland is noted in the dog even after denervation or extirpation of the adrenals and in the frog after cauterization or extirpation of these glands.

HERRON, Spokane, Wash.

PROTAMINE INSULIN (LEO-RETARD) IN CHILDHOOD DIABETES. L. FREY, Arch. f. Kinderh. **109:**228, 1936.

On the basis of his experiences in the use of protamine insulin in four cases of juvenile diabetes, Frey believes that the drug represents a marked advance in insulin therapy for the diabetic child.

CRANE, Washington, D. C.

RELATIONSHIP OF THE THYROID GLAND TO BONE REGENERATION. H. HANKE, Deutsche Ztschr. f. Chir. **247:**317 (July 30) 1936.

Hanke studied healing in rabbits following experimental surgical removal of sections of bone. Apparently thyroidectomy has practically no effect on bone regeneration. In the absence of the thyroid gland a strong callus is formed, and healing takes place practically as rapidly as before the thyroid was removed. In normal animals from which the thyroids have not been removed, daily parenteral injection of a thyroid extract causes significant stimulation of bone regeneration. The callus is stronger and is formed more rapidly. It is concluded that the thyroid gland, unlike vitamin C, is not necessary for bone regeneration. Observations on cretins and in persons with hypothyroidism are in agreement with this. In normal growing animals administration of thyroid causes general cellular stimulation, resulting in more rapid formation of bone. However, observations on man must show under what conditions administration of thyroid is indicated if the fragments are in good position.

GLASER, Rochester, N. Y.

HYPOPHYSOMETRY. H. W. REICH, Fortschr. a. d. Geb. d. Röntgenstrahlen **54:** 381 (Oct.) 1936.

Reich describes an instrument for measuring various dimensions of the roentgen projection of the sella turcica and points out the advantages to be gained by the use of the device. In the paper which follows this one (p. 386) Bober reports results obtained with the instrument.

MCCUNE, New York.

ABSCESS TONSILLECTOMY IN DIABETES. J. SCHUBEL, Ztschr. f. Hals-, Nasen- u. Ohrenh. **39:**427, 1936.

Schubel maintains that abscess tonsillectomy is not serious for a normal organism. On the contrary, observations on several hundred persons have proved that it is the method of choice. However, there remains the question whether this procedure is advisable for the patient with a systemic disorder, such as diabetes. A girl aged 17 had been diabetic since the age of 14. She was brought to Schubel's clinic on account of a peritonsillar abscess that had existed for three days. She was in a precomatose stage, and the question arose whether the operation should be postponed and the diabetes treated first or whether an operation should be performed in spite of the precoma. Since postponement of intervention involved the danger of tonsillogenic sepsis, it was decided to resort to abscess tonsillectomy under local anesthesia. After the intervention the patient stated spontaneously that she felt greatly relieved. Then measures were taken to counteract the coma. They were successful, and the daily treatment of the tonsillectomy wound revealed that the healing took a normal course. This case convinced Schubel that abscess tonsillectomy in a patient with diabetes involves no greater risk than a less extensive intervention done under local anesthesia.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CHANGES IN THE BLOOD CHEMISTRY IN PARATHYROID TETANY AND FOLLOWING ADMINISTRATION OF PARATHORMONE. S. SIWE, Ztschr. f. Kinderh. **57**:383 (Sept. 19) 1935.

Because of the theoretical discussion of the results, the article does not lend itself to abstracting. Siwe reports studies on calcium and phosphorus in six other articles in the same number of the *Zeitschrift für Kinderheilkunde*.

SIEMSEN, Chicago.

INVESTIGATIONS REGARDING THE CARBOHYDRATE HORMONE OF THE ANTERIOR LOBE OF THE PITUITARY IN THE BLOOD IN GLYCOGEN STORAGE DISEASE. W. HERTZ, Ztschr. f. Kinderh. **57**:525 (Dec. 12) 1935.

It is assumed that the anterior lobe of the hypophysis secretes a carbohydrate hormone which has the important function of mobilizing glycogen from the liver. Hertz was able to confirm the findings of others that blood serum taken from normal persons after ingestion of a large amount of carbohydrate, when injected into rats "deglycogenizes" the liver. Blood serum from two patients with glycogen storage disease had the same effect. On the basis of Hertz' work there is no definite evidence that the hormone is missing in this disorder.

SIEMSEN, Chicago.

THE EFFECT OF THE FUNCTIONAL ABNORMALITY OF THE MATERNAL THYROID ON THE GENITAL GLAND OF THE FEMALE FETUS. T. TANIOKA, Jap. J. Obst. & Gynec. **19**:393 (July) 1936.

Tanioka studied twelve rabbits, using four as a control series, removing the thyroid from five and feeding a total of from 0.3 to 0.9 Gm. of powdered thyroid in divided doses during pregnancy to the remaining three. A slight average decrease in birth weight of the offspring occurred both in the thyroidectomized animals and in those fed thyroid. The ovaries showed less decrease in weight than did the body as a whole.

ADAIR and POTTER, Chicago.

ADRENAL TUMOR IN A CHILD. G. HEDERSTAD, Nord. med. tidskr. **12**:1795 (Oct. 31) 1936.

A boy aged 13 was first seen in 1932. Accidentally a tumor was demonstrated under the left border of the ribs. This tumor was diagnosed roentgenologically as belonging to the left kidney. At the subsequent laparotomy it was found to be inoperable. Some weeks later the boy began to suffer from pains in his left side, and his general condition grew worse. In 1933 the sight of his eyes was impaired by hemorrhages and edema of the retina. There was protrusion of the eyeballs. The blood pressure was 200. The nonprotein nitrogen was 60 mg. per hundred cubic centimeters. The urine showed no changes. Secondary anemia was present. There were several tumor-like nodules on the skull and sternum. The boy died in 1934. Postmortem examination disclosed an adrenal tumor on the left side with metastasis in the skull and sternum. Histologically it was a sympathoblastoma.

WALLGREN, Göteborg, Sweden.

APPLICATION OF PROTAMINE INSULIN IN DIABETES MELLITUS IN CHILDHOOD. J. VAN LOOKEREN CAMPAGNE and J. P. BOEKHOLD, Maandschr. v. kindergeneesk. **5**:487 (Sept.) 1936.

Experience in five diabetic children showed that protamine insulin is very useful when a preparation is wanted which will show retarded activity.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Muscles, Bones, Joints and Lymph Glands

A Study of "Simple Disuse Atrophy" in the Monkey. H. Chor and R. E. Dolkart, Am. J. Physiol. **117**:626 (Dec.) 1936.

Body and leg casts were applied to young monkeys (Macacus rhesus), and chemical and histologic studies were made on the gastrocnemius and soleus muscles after varying periods of inactivity. Gross evidence of a decrease in muscle bulk was evidenced after one week and increased during longer periods of immobilization. The authors conclude that atrophy from disuse is a distinct entity and is simple in character, as revealed by histologic examination. It consists primarily of a uniform reduction of the bulk of each muscle cell, specially of the sarcoplasm. It is not attended by any evidence of degeneration or by attempts at regeneration. Irritability to electrical stimuli remains unaffected. There is no alteration in the proportions of water and nitrogen. It is not associated with any demonstrable changes in the anterior horn cells of origin of the respective nerve supply.

Nourse, Cleveland.

Psychic Factors in Rheumatoid Arthritis. G. Thomas, Am. J. Psychiat. **93**:693 (Nov.) 1936.

Twenty cases of rheumatoid arthritis of varying degree and duration with an age range between 11 and 67 years are described. In every case there was a history of emotional struggle preceding the attack. In some instances, particularly among the juvenile patients, the rheumatoid arthritis displaced the psychic symptoms.

Jahr, Omaha.

Physical Deformities Commonly Regarded as Due to Rickets. E. Pritchard, Brit. J. Phys. Med. **11**:102 (Oct.) 1936.

The diagnosis of rickets on the basis of clinical signs, such as bandy legs, knock knees, lordosis, kyphosis, flatfoot and pigeon chest is deplored. Pritchard emphasized that many are congenital, that others are familial and that some are due to mechanical effects of laxity of ligaments and muscular weakness. He describes and illustrates an apparatus consisting of pads mounted on a spring which encircle the chest for the correction of pigeon chest.

Hartman, Cleveland.

Ossification of a Cephalohematoma. Digonnet, Bull. Soc. d'obst. et de gynéc. **25**:459 (June) 1936.

The patient was a girl who weighed 3,100 Gm. at birth, following a normal delivery. The next day a cephalohematoma of the right parietal region was noted. This was present when the patient was discharged at the age of 11 days. At the end of seven weeks the child was brought back to the clinic. The cephalohematoma then measured 7 by 6 cm. and was 2 cm. in height. It was of osseous consistency, and the surface was somewhat irregular. A roentgenogram (reproduced in the text) confirmed the clinical diagnosis of an ossified cephalohematoma. The infant presented no other abnormality. Digonnet comments on the great rarity of this condition and in spite of this case still favors the classic method of treatment of cephalohematoma, i. e., letting nature take its course, as opposed to the method of puncture, drainage and application of a tight compress.

Glaser, Rochester, N. Y.

A Case of Congenital Chondrodystrophy. Anastasio Vergara E., Rev. mex. de puericultura **5**:950 (Dec.) 1935.

The author reports and discusses a case.

Herron, Spokane, Wash.

HYPERPLASTIC PERIOSTITIS IN A THREE MONTH OLD PREMATURE INFANT. A. MEIER, Arch. f. Kinderh. **109**:223, 1936.

A case is reported of hyperplastic periostitis in a 3 month old premature girl with a congenital heart defect. The findings increased in intensity up to the age of 6 months, then gradually receded. There was simultaneous improvement in the cardiac condition.

CRANE, Washington, D. C.

CLINICAL ASPECTS OF OSTEOPSATHYROSIS. E. RUTTIN, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **141**:43, 1936.

Ruttin states that in 1922 he reported five cases of osteopsathyrosis and that since then he has observed five others. He cites the ages at which hardness of hearing was first noted. He investigated this to learn whether in such cases the hardness of hearing begins earlier than in ordinary otosclerosis. In the majority of cases the onset occurred at about the same time as in ordinary otosclerosis. However, it appears that in osteopsathyrosis the otosclerosis progresses more rapidly to a severe degree. As to the relationship of the time of the fractures to that of the onset of otosclerosis, he says that the fractures took place earlier. Whereas the fragility of the bones is greatest during childhood and decreases with advancing years, the otosclerosis shows the opposite behavior in that it increases with advancing years. From the clinical standpoint, the three main symptoms of osteopsathyrosis (blue scleras, fragility of the bones and hardness of hearing) are not equivalent. The blue scleras are apparently already present during the fetal stage and later remain about the same; the fragility of the bones likewise begins during the fetal stage and decreases gradually during the post-fetal period, but the otosclerosis, for which only a predisposition exists, does not begin until about the time of puberty.

The author emphasizes that although both osteogenesis imperfecta and osteopsathyrosis idiopathica have been regarded as a constitutional anomaly of the mesenchyme and of all its derivatives, it is nevertheless necessary to make a clinical differentiation between these two conditions. Regarding the heredity of osteopsathyrosis, he says that his earlier material indicated that a parent with all three anomalies may have offspring with all three or only one or two, but a parent with only one or two anomalies does not have offspring with all three. In the newer material, however, it was found that even parents without any of the defects may have offspring with all three. In the case under consideration, the grandfather had had the defects.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF THE KLIPPEL-FEIL ANOMALY OF THE CERVICAL PORTION OF THE SPINE. T. CANIGIANI, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:296 (Sept.) 1936.

The Klippel-Feil anomaly of the cervical vertebrae is a true developmental defect. Roentgenographically, it is characterized by morphologic immaturity of the vertebral bodies and by fusion of the bodies one with another. The obvious clinical feature is shortening of the neck; other developmental anomalies are apt to be present. Care must be taken to distinguish between the deformities due to the Klippel-Feil anomaly and those which result from healed tuberculosis of the cervical spine. The latter may also produce fusion of the vertebral bodies; it has been designated the "pseudo-Klippel-Feil phenomenon." The two conditions are most conclusively differentiated by roentgen examination.

McCUNE, New York.

ROENTGEN TREATMENT OF MYOSITIS OSSIFICANS MULTIPLEX PROGRESSIVA. M. SGALITZER, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:304 (Sept.) 1936.

The cases of progressive multiple ossifying myositis reported up to the present time number approximately 150. The condition must be differentiated from

localized myositis ossificans, which is the result of trauma; also, from multiple osteomas, with which it has been classified since the time of Virchow. It occurs principally in children. Since the victims usually die early in life of intercurrent infection, the disorder is seldom seen after the twentieth year of life. The cause is unknown, although constitutional predisposition probably plays an important part: Many of the patients exhibit associated anomalies of development. The pathogenesis of the ossifying changes is poorly understood; the fundamental aberrations are probably more closely related to the intermuscular connective tissue than to the muscle fibers themselves. The results of various types of treatment, including surgical removal of the pathologic bone and partial parathyroidectomy, have proved disappointing.

Two cases are reported. The first is that of a 13 year old girl and the second that of a 10 year old girl. The first patient received no treatment. The second received extensive roentgen therapy, which appeared to produce gratifying results. The details of treatment are supplied, and a useful bibliography is appended.

McCune, New York.

Luschka's Deformity and Other Anomalies of the Ribs. O. Schedtler, Röntgenpraxis **8**:527 (Aug.) 1936.

The ribs are frequently the site of congenital anomalies. Some of these, such as congenital absence of one or more ribs, may be accompanied by congenital absence of the pectoralis major muscle. Others occur independent of associated anomalies and can be detected only by roentgen examination. A deformity which is by no means rare is that described by Luschka. It consists of a shovel-like widening of the sternal end of one or more ribs; in some cases a broad cleft is present in the midportion of the expanded area. The fourth rib is most commonly affected, and the anomaly may be bilateral. Serb's name is associated with a third type of anomaly which consists of partial fusion of two contiguous ribs, usually the first and second. To the list may be added cervical rib and anomalous calcification of the costal cartilage. Schedtler found twenty examples of these anomalies in roentgen films made on 935 patients. Luschka's deformity was the commonest.

McCune, New York.

Bipartite First Cuneiform Bone. E. Heidsieck, Röntgenpraxis **8**:712 (Oct.) 1936.

Congenital partition of the first cuneiform bone into separate halves is rare. However, when it occurs it runs true to form: The cleft between the two portions is always in the horizontal plane, parallel to the plantar surface. The evenness of the line of cleavage and the regularity of the outlines of the component halves distinguish this partition from fracture due to trauma. The anomaly is sometimes accompanied by symptoms of discomfort in the feet; in some cases the discomfort is one-sided, although the lesion is bilateral. A case is reported. The bibliography is useful.

McCune, New York.

Pathologic-Anatomic Investigation Regarding the Nature of Osteogenesis Imperfecta. K. L. Winkelmann, Ztschr. f. Kinderh. **58**:1 (May 20)) 1936.

Different findings and views encountered in the literature are cited and compared. Detailed pathologic anatomic studies in a case of osteogenesis imperfecta revealed findings conforming to an early period of fetal development. Winkelmann concludes that the disorder represents arrested or retarded osteogenesis and that, if the patient's life is carefully guarded, especially by avoidance of respiratory infections, the chances of recovery are good.

Siemsen, Chicago.

MUSCULAR FUNCTION IN PROGRESSIVE MUSCULAR ATROPHY. J. CSINÁDY and G. PETRÁNYI, Orvosi hetil. **80**:1133 (Nov. 28) 1936.

The so-called ergometrographic procedure is useful in determining the strength and the work of the muscles in progressive muscular atrophy. Long observation of two children with this condition showed that their muscle work was only from 8 to 9 per cent of that of normal children. It is well known that a spontaneous remission can occur. Such a remission can be shown by this method much earlier than the clinical symptoms show it. The results of the combined treatment with amino-acetic acid, epinephrine and pilocarpine can be shown exactly by this method.

GÖTTCHE, Budapest, Hungary.

CALCIUM AND PHOSPHORUS CONTENT OF THE VIOSTEROL SHADOWS IN BONES. T. YOSHINARE, J. Pediat. (Tokyo), no. 438, Nov. 20, 1936, p. 1513.

The author made quantitative estimations of the calcium and phosphorus in the diaphyses of long bones in which after administration of viosterol increased transverse shadows developed as shown on roentgenograms. He found the two elements to be definitely above normal. Compared with the results of similar analyses in cases of lead poisoning, however, the quantities of both calcium and phosphorus in viosterol-treated animals were lower. Identical results were obtained from quantitative analyses of the bones of a viosterol-fed infant aged 7 months. From these observations the conclusion is reached that increased amounts of calcium and phosphorus play a significant rôle in the increased density of the diaphyses of long bones so frequently observed in persons fed viosterol as well as in those poisoned with lead.

KATO, Chicago.

OSTEOCHONDRITIS ISCHIOPUBICA. J. TORGERSEN, Norsk mag. f. lægevidensk. **97**: 951 (Sept.) 1936.

The cases of two children, aged 8 and 9 years, respectively, are reported. The children had an involvement of the synchondrosis between the os pubis and the os ischii. Roentgenologic examination displayed a nut-sized swelling of the synchondrosis, which was sclerotic at its border and vacuolated in its center. The disease is considered to be an illness sui generis. The symptoms are pains in the lumbar region, and the disease affects children in whom the synchondrosis is ossifying, especially children in whom there is marked asymmetry of the ossification.

WALLGREN, Göteborg, Sweden.

STILL'S DISEASE WITH NODULES. J. VAN AARDENNE, Maandschr. v. kindergeneesk. **5**:494 (Sept.) 1936.

This article includes a description of a case of Still's disease in a boy 1½ years old with nodules on the head and back and an extensive discussion of all the particularities which may appear in this disease. The results of the histologic investigation of one nodule and of one lymph gland are given.

VAN CREVELD, Amsterdam, Netherlands.

CHONDRODYSPLASIA (OLLIER'S DISEASE). H. R. BAX, Nederl. tijdschr. v. geneesk. **80**:5192 (Nov. 21) 1936.

This is a description of a case of chondrodysplasia (Ollier's disease) in a girl of 1 year. The peculiar form of the foci in the wings of the iliac bone deserves attention. This lends support to the theory proposed by Bentzon (1924), who surmises a connection between these lesions and the course of the nutrient vessels of the bones.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Eye

MASSIVE RETINAL FIBROSIS IN CHILDREN. A. B. REESE, Am. J. Ophth. **19**:576 (July) 1936.

Reese encountered in young persons several conditions characterized by protrusion of a grayish white mass from the retina as a result of organization of a hemorrhage occurring at birth or resulting from trauma after birth. He reports three cases, giving the clinical and pathologic findings, and states:

"Retinal hemorrhage in children can organize into a fibrous mass resembling clinically a retinoblastoma. Owing to contracture, more and more of the retina can be pulled into the lesion, giving it the appearance of progressing and thereby leading all the more to the suspicion that it is a retinoblastoma. There is usually no detachment of the retina, because the lesion is adherent to the choroid. The retinal hemorrhage occurs at birth from the same conditions that produce the analogous condition of massive intracranial hemorrhage. It may occur as the result of trauma in early childhood."

REESE, Philadelphia. [ARCH. OPHTH.]

CONGENITAL FAMILIAL OPHTHALMOPLEGIA. P. BONNET and L. PAUFIQUE, Ann. d'ocul. **173**:135 (Feb.) 1936.

Bonnet and Paufique report the case of a family in which the father and three children suffered from complete bilateral external ophthalmoplegia. The father, one of eleven brothers and sisters, was the first member of the family known to have the disease. Of the thirty-three members of the second generation, only the three children of this patient were affected. The signs were those of complete bilateral external ophthalmoplegia; ptosis was marked, and the eyeball was usually turned down and fixed. Rotary nystagmus was present, and convergence was paralyzed. Attempts to look up were followed by a quick movement of convergence, which was immediately replaced by nystagmus. Neither strabismus nor diplopia was present. Beside refractive changes, which varied in each patient, and changes in the fundus, which could not be studied properly because of the difficulties of examination, no other concomitant anomaly existed. The intelligence of the patients was normal.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

HERPES ZOSTER OPHTHALMICUS PRECEDED BY OCULAR SYMPTOMS. BUSSY and BONAMOUR, Ann. d'ocul. **173**:477 (June) 1936.

Bussy and Bonamour report the case of a child aged 7½ years who had had interstitial keratitis with folds in Descemet's membrane. These ocular disturbances were observed several days before the appearance of herpes zoster ophthalmicus in the area supplied by the nasal and infra-orbital nerves.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

BILATERAL PUPILLARY ANOMALIES; PERSISTENCE OF THE ANNULAR SINUS. V. VILLARD and H. VIALLEFONT, Bull. Soc. d'opht. de Paris, April 1936, p. 317.

A girl of 13 years had noted a peculiar appearance of her eyes for many years. On examination one was impressed by an anomaly of the pupil and iris. Externally the chestnut-colored iris was perfectly normal, but the internal portion, which was seen best with the slit lamp, showed a border from 0.3 to 0.5 mm. wide, forming a complete circle of blackish brown, the classic color of the uveal pigment. At a distance this anomaly made the eyes appear as though the pupillary borders were markedly irregular, the usual curved pupil appearing serrated. Photographs and drawings of the condition are shown. Szili and Gallenga have reported like conditions. The anomaly was evidently caused by a developmental failure of the pigment of the iris to cover that of the uvea.

MAYER, Chicago. [ARCH. OPHTH.]

FAMILIAL MACULAR DEGENERATION OF UNKNOWN CAUSE. H. TILLÉ, Bull. Soc. d'opht. de Paris, July 1936, p. 548.

In two young girls, sisters, of a family of eight children, bilateral macular degeneration, which had begun apparently at birth, had resulted in loss of central vision. Tillé feels that this condition does not fit in with that described as due to syphilis by Morax in France, with that due to tuberculosis as shown by authorities of central Europe or with that caused by abiotrophy or focal infection as described by North American writers. Photographs of the macular regions of both patients are shown. All physical examinations showed no evidence of disease, and the antecedents in two previous generations had normal eyes. Treatment was of no avail. Tillé is unable to classify the lesion in these patients with any reported in the previous literature, which he reviews.

MAYER, Chicago. [ARCH. OPHTH.]

TREATMENT OF TRACHOMA IN CHILDREN. WIBAUT, Rev. internat. du trachome **13**:174 (Oct.) 1936.

The prognosis for the cure of trachoma in children is much better than that for the cure of trachoma in adults. The requirements are early detection and prolonged and prudent treatment. Children under 5 years of age may show only suspicious thickening of the conjunctival epithelium, but between the ages of 5 and 10 years follicles are generally well developed. These follicles should be attacked by expression, and frottage with a 1 per cent solution of silver nitrate or some other suitable medicament should be continued for a few months thereafter. Strong caustics are to be avoided, and operation is seldom necessary.

LEBENSOHN, Chicago. [ARCH. OPHTH.]

VON HIPPEL'S DISEASE; LINDAU'S DISEASE: I. H. VIALLEFONT, Rev. d'oto-neuro-opht. **13**:405 (June) 1935.

Viallefont has collected all that has been published on von Hippel's disease. This name is applied to isolated angiomatosis of the retina, while "Lindau's disease" is reserved for retinal angiomatosis associated with angioma of the nervous system and with visceral malformations. These diseases are compared with Bourneville's disease, Recklinghausen's disease and the encephalotrigeminal angiomatosis of Crouzon. Von Hippel published his observations in 1926, and in 1927 Lindau called attention to the coincidence of retinal angiomatosis and cyst of the cerebellum. The evidence shows that the condition is not local but is a malformation of vascular tissue involving the central nervous system, the retina and even all organs of the body. Its hereditary and familial character is emphasized. Cushing and Bailey were the first to diagnose Lindau's disease clinically. The close relationship of Lindau's disease, Bourneville's disease (tuberous sclerosis of the cerebral convolutions), encephalotrigeminal angiomatosis, Recklinghausen's disease and phakomatosis of van der Hoeve is pointed out. The familial character of this whole group of diseases has been demonstrated by Ley, van Bouwdijk, Bastiaanse, van Bogaert, Guillain and Lagrange, Bielschowsky, van der Hoeve and Nieuwenhuyse. Embryologically, there is a close relation between the branches of the trigeminal nerve and the vascular trunks from the internal carotid artery. It is therefore easy to conceive of localization of angiomatous formations both in the skin and in the meningeal territory of the trigeminus nerve. Oppenheif observed a child with nevus of the face, convulsive crises and three round tumors of the retina.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

VON HIPPEL'S DISEASE; LINDAU'S DISEASE: II. H. VIALLEFONT, Rev. d'oto-neuro-opht. **13**:485 (July-Aug.) 1935.

In this article Viallefont discusses together von Hippel's disease and Lindau's disease. Retinal angiomatosis is rare. It affects young persons (before the age of 25 years) by predilection. It is not congenital, however. It attacks the two

sexes with equal frequency. The most striking factor in the etiology of the pure or the associated form of angiomatosis is its familial and hereditary character. In the beginning it is unilateral, and a long interval intervenes before the second eye is involved. Visual acuity diminishes little by little, with an accompanying narrowing of the visual field, at times with scotoma. The eyeground has a pale orange tint. Optic neuritis may occur early. In the manifest stage the subjective symptoms are more marked; examination of the eyegrounds reveals tortuous, dilated vessels in pairs, extending from the papilla to the periphery; intercalated in the circulatory circuit is a round tumorous yellowish red mass, which projects above the retinal surface. The eye may contain several such units as the disease evolves. Surrounding the masses are whitish patches (proliferation of benign character), which may mask the original lesion and extend to the maculopapillary region; they represent a glial reaction and are secondary to the angiomatous process. Complications include localized or profuse hemorrhages, detachment of the retina, glaucomatous attacks and choroidal cataract. The proliferated reticular cells are often attacked by xanthomatous or cystic degeneration. Extra-ocular lesions are observed in the nervous system (in the cerebellum, vicinity of the fourth ventricle, bulb and spinal cord). Lesions in the cerebellum are usually single. Histologically, the angiomatous tumor is formed by capillaries, among which are cells which Lindau, Cushing and Bailey stated to be of endothelial origin (angioreticuloma). When the intervascular cells are of glial origin, the tumor is called angioglioma. The angioreticuloma evolves by fibrous alteration of the reticular stroma or by xanthomatous or cystic transformation. Visceral lesions are situated in the pancreas, kidneys and adrenal glands; they are cysts, the walls of which are formed by cuboid or squamous cells of the endothelial type. Lesions of the liver, ovaries and bones have been observed. Many and varied theories of the pathogenesis of Lindau's and von Hippel's disease have been voiced. Viallefont confesses complete ignorance of the intimate pathogenic processes involved in pure or associated retinal angiomatosis.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

PATHOGENESIS OF HYDROPHTHALMOS. A. SANTONASTASA, Ann. di ottal. e clin. ocul. **64**:405 (June); 437 (July) 1936.

The literature on the pathogenesis of hydrophthalmos, especially that dealing with the histopathologic aspects, is reviewed. Thirteen cases are reported, including one in which the condition was studied histologically at an early stage. The patient was a child of 5 years whose mother had been treated for syphilis during lactation. The right eye had begun to increase in size at the age of 4 months. The blood of the mother and that of the child gave a positive Wassermann reaction. The corneal diameter measured 17 mm., and the tension was 52 mm. Vision was nil. The left eye was normal. Section of the right eye showed absence of Schlemm's canal, with the usual changes due to distention of the globe. There were slight inflammatory changes, with infiltration of the iris and ciliary body and marked endarteritis of all the vessels. In nine of the cases the condition was bilateral, and in nine it occurred in males. In one case in which the hydrophthalmos was bilateral a vascular nevus of the face was present on one side, while in one case in which the condition was unilateral it was evidently secondary to interstitial keratitis. Among four cases in which Wassermann tests were made, in only one was there a positive result, but in five cases it was considered that syphilis was probably present in the parents or children.

Santonastasa believes syphilis to be an important cause of hydrophthalmos. In his case sections indicated that a canal of Schlemm may have been present but was obliterated by inflammatory changes, and he considers that the findings in other reported cases of hydrophthalmos may be interpreted in the same way. Photographs, photomicrographs and a bibliography accompany the article.

GIFFORD, Chicago. [ARCH. OPHTH.]

MULTIPLE PIGMENTED CONGENITAL CYSTS OF THE IRIS. J. A. SENÁ, Arch. de oftal. de Buenos Aires **11**:462 (Aug.) 1936.

After giving a detailed classification of cysts of the iris according to their origin, with abundant bibliographic references, Sená stresses the production of spontaneous intra-epithelial cysts due to nonfusion of the two layers of the epithelium of the iris and reports a case of multiple cysts of this nature near the pupillary margin in each eye. A stereophotograph and a colored drawing illustrating the condition are included. FINLAY, Havana, Cuba. [ARCH. OPHTH.]

DEVELOPMENT OF COLOR PERCEPTION IN CHILDHOOD. A. NEVES, Arch. de pediat., Rio de Janeiro **9**:63 (Dec.) 1936.

The physiologic aspect is discussed. SANFORD, Chicago.

KERATOMALACIA. L. HOLTHAUSEN, Arch. f. Kinderh. **109**:34, 1936.

A case is reported of keratomalacia and xerophthalmia in an extremely malnourished infant. CRANE, Washington, D. C.

EYES AND SPORT. W. ROHRSCHNEIDER, Med. Klin. **32**:1040 (July 31) 1936.

Rohrschneider presents an elementary discussion of some of the conditions which may affect the eyes of athletes. DOOLEY, New York.

RELATION BETWEEN ZONULAR CATARACT, RICKETS AND TETANY. G. VON BAHR, Nord. med. tidskr. **12**:1479 (Sept. 5) 1936.

Von Bahr quotes the present valid opinions on the relation between zonular cataract, rickets and tetany and calls attention to the fact that it is still dubious whether rickets or tetany is the cause of the cataract. In order to solve this problem he studied the development of zonular cataract in rachitic mice with and without tetany. The Steenbock-Black rachitogenic diet was given to 109 mice. After three weeks or more, roentgen examination of the knee joints showed rickets. Then the diet of 65 of the animals was changed in such a manner that the ratio of calcium to potassium was 1:1 instead of 4:1 as previously. Through this change in the diet the galvanometric irritability of the nerves was increased, and some of the mice showed tremor, rigidity of the muscles or tetanic convulsions. At the same time punctiform opacities of the lens capsule developed in several animals. This lesion of the lens was observed, in all, 49 times in 109 rachitic mice, and, of these 49 animals, 48 belonged to the group which had their ratio of calcium to potassium changed to 1:1. Twenty-nine control mice, which received a normal diet and had no rickets, got the same ratio of calcium to potassium without development of any cataract. Thus, in rachitic mice a diet producing tetanic symptoms often causes a cataract, while there is no reason to believe that simple, uncomplicated rickets can cause a cataract. WALLGREN, Göteborg, Sweden.

RELATION BETWEEN THE GENERAL STATE OF HEALTH AND THE INCIDENCE OF MYOPIA IN SCHOOL CHILDREN. G. NORDGREN, Nord. med. tidskr. **12**:2069 (Sept. 19) 1936.

Nordgren studied the incidence of myopia in Swedish school children during the period from 1894 to 1935. There were 30 per cent fewer myopic children in 1920 than in 1894. In 1920 the incidence of myopia steadily increased with increase in age from 3.7 per cent in the first class at school to 19.1 per cent in the last one; in 1894 the corresponding figures were 5.2 and 24.6 per cent. There is positive evidence of correlation between the frequency of a general bad state of health and the frequency of myopia. This indicates either that there is similar

predisposition to these conditions in the individual patient or that exogenous factors which produce myopia produce many other ailments. The author's analyses suggest that children who live under bad hygienic conditions are more liable to contract myopia than those living under good conditions. No doubt, both endogenous and exogenous influences are active in the development of myopia. It is very probable that the incidence of myopia can be greatly reduced by amelioration of the hygienic conditions in schools and in the homes of the children.

WALLGREN, Göteborg, Sweden.

Skin Diseases; Allergy

ALUM AS AN ADJUVANT IN SENSITIZING GUINEA-PIGS TO RAGWEED POLLEN (AMBROSIA ARTEMISIIFOLIA). A. H. W. CAULFEILD, M. H. BROWN and E. T. WATERS, J. Allergy **7**:541 (July) 1936.

Sensitization, as judged by anaphylactic shock, was increased by using an alum-precipitated extract of ragweed pollen subcutaneously in guinea-pigs. Sensitization was much more constant and of greater degree than when a solution of ragweed pollen protein or a 5 per cent aqueous extract of ragweed pollen previously defatted with ether was used. It is possible that the slow absorption of the antigen caused by the alum allows the stimulus to act over a longer period and thus increases the sensitivity.

HOYER, Cincinnati.

ALLERGIC SHOCK. M. PIERSON, J. Michigan M. Soc. **35**:699 (Nov.) 1936.

This article is a brief summary of the data on six cases recently seen.

CAREY, Detroit.

FLAT HEMANGIOMA OF THE FACE TREATED BY FREEZING. A. MARIN, Union méd. du Canada **65**:446 (May) 1936.

A baby of 6 months had an extensive hemangioma involving the left side of the face—the cheek, upper lip and eyelids, whence it extended onto the nose and forehead. Tuberous portions were treated by radium puncture, and treatments with carbon dioxide snow were started over the remainder. At the age of 2½ years, the child showed practically no residuum.

Treatments were given every fifteen days during the first year and every three or four weeks during the second. Marin feels strongly that treatment should be started as early as possible.

DAFFINEE, Boston.

ECZEMAS OF INTERNAL ORIGIN. R. O. HALLORAN, West Virginia M. J. **32**:311 (July) 1936.

Halloran presents an interesting and pleasing review of eczema of children due to internal causes and discusses the etiologic factors, treatment, etc., but makes no attempt to present anything especially new or unusual.

SHAWKEY, Charleston, W. Va.

URTICARIA PIGMENTOSA WITHOUT PIGMENTATION. A. SÉZARY and A. HORWITZ. Bull. Soc. franç. de dermat. et syph. **43**:78, 1936.

The authors report a case of urticaria characterized by infiltration of mast cells in the cutis but lacking the ordinary pigmentation which accompanies this dermatosis. The eruption was of nine months' duration and was characterized by red papules which urticated on friction and by dermographism in apparently normal skin. The authors hesitated to make a clinical diagnosis of urticaria pigmentosa without pigmentation and made the decision only after a biopsy had been done.

In discussing the case Simon stated that in his opinion too much attention was being attached to the histologic structure of dermatologic lesions, this leading to diagnoses which were an insult to grammarians and scientific men, such as urticaria pigmentosa without pigmentation and aleukemic leukemia. Thiebault agreed with his view.

LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

A CASE OF ONYCHORRHEXIS WITH RECOVERY. L. CAZAC AVERBUCH, Bull. Soc. de pédiat. de Iasi **6**:91 (Oct.-Dec.) 1935.

A boy, first observed at 12 years of age, when he showed definite psoriasis and onychorrhexis, was given anterior pituitary extract for three months in 1933, with no improvement. In 1934, he received thyroid and testicular extract for six months. At the end of this time the testicles descended, and simultaneously the psoriasis disappeared and the nails improved. At presentation of the case, in December 1935, the nails were normal.

LESLIE, Evanston, Ill.

GENERALIZED INTERSTITIAL CALCINOSIS IN A CHILD 5½ YEARS OF AGE. W. PIAGGIO GARZÓN and J. A. SOTO, Med. de los niños **37**:6 (Jan.) 1936.

The child presenting generalized calcinosis had a stormy first year, with frontal sinusitis, protracted vomiting and other nutritional disturbances. As a stimulant to nutrition she was given decalose (a solution of calcium chloride and calcium lactate, chemically pure). Three years later subcutaneous nodules appeared, which biopsy proved to be calcified. There was no discoloration of the skin, palpation was not painful, and the nodules were freely movable in the skin and in the deeper planes.

The urine was normal. The Wassermann reaction was negative. On several occasions the blood showed from 11 to 12 mg. of calcium and from 3 to 4 mg. of phosphorus per hundred cubic centimeters.

The authors give a brief review of the literature on disturbances of calcium metabolism as influenced by parathyroid hormone, vitamin D, phosphorus and ultraviolet rays. In the authors' case the deposition of calcium in the tissues continued rapidly, despite the several methods of treatment carried out.

DWYER, Kansas City, Mo.

A CASE OF ERYTHEMA ANNULARE. B. SCHMIDEK, Med. Klin. **32**:1048 (July 31) 1936.

This report concerns a 4 year old child who was being followed in the clinic because of cervical adenitis and in whom erythema annulare was seen to develop five days before the first signs of acute rheumatic endocarditis with pains in the joints. The case would not be noteworthy except that the child was so young and that the cutaneous lesions appeared before the signs of involvement of the heart or the joints.

DOOLEY, New York.

NEUROFIBROMATOSIS OF RECKLINGHAUSEN. E. HAINISS, Orvosi hetil. **80**:1201 (Dec. 19) 1936.

A 14 year old girl had a thickening on her left leg from birth. This leg grew shorter. The skin of the left femoral region was soft and flabby and could be raised in many wrinkles. This skin showed great pigmentation, and the whole body was covered with coffee-colored patches varying in size from that of a pear to that of a quarter-dollar and especially plentiful on the face, neck, back and chest. The bones showed decided roentgen changes. Histologic examination of an area of skin cut out from the femoral region confirmed the diagnosis. Mental deficiency was not present—merely a slight inclination to psychic depression.

GÖTTCHE, Budapest, Hungary.

HYPOTHERMIA AND EDEMA. J. MUNK, Maandschr. v. kindergeneesk. **6**:12 (Oct.) 1936.

This is a description of five cases of hypothermia in young infants. The edema occurring in such infants is explained by an insufficiency of the kidneys.

VAN CREVELD, Amsterdam, Netherlands.

MACULAR TYPE OF BULLOUS HEREDITARY DYSTROPHY. L. L. CAROL and R. KOOY, Maandschr. v. kindergeneesk. **6**:39 (Nov.) 1936.

A study was made of several affected members of the second generation of a family with bullous hereditary dystrophy, a disease described in 1908 by Mendes da Costa and van der Valk. It is remarkable that one of the most prominent symptoms, the bullae, was never present when the children were carefully treated in the hospital but always appeared when they were at home. Injections of a preparation called ambinon (said to contain the thyrotropic and gonadotropic hormones of the anterior lobe of the hypophysis) improved the hair growth temporarily.

VAN CREVELD, Amsterdam, Netherlands.

ERYTHEMA NODOSUM WITH NEGATIVE TUBERCULIN TESTS. T. HALBERTSMA, Maandschr. v. kindergeneesk. **6**:113 (Dec.) 1936.

Next to the erythema nodosum closely related to tuberculosis exists another form with a quite different etiology. Halbertsma describes some cases of the last-mentioned form. Two of these cases were in sisters who had erythema nodosum at the same time; in one girl it developed in connection with beginning tuberculous peritonitis; in the other, without any tuberculous infection. Even after eleven years the Pirquet and Mantoux tests of the latter patient still were negative. Another case was that of a child of a mother who died of tuberculosis; in the child with erythema nodosum the tests for tuberculosis were repeatedly negative.

VAN CREVELD, Amsterdam, Netherlands.

ALLERGIC EDEMA (QUINCKE) ACCOMPANIED BY A PARTICULAR NECROSIS. C. E. BENJAMINS, Nederl. tijdschr. v. geneesk. **80**:3332 (July 18) 1936.

Benjamins reports a case of Quincke's edema in a boy of 9 years, who had in the region of the edema a round firm swelling in the subcutaneous tissue. At the microscopic examination of the surgically removed swelling a strong infiltration with leukocytes, especially with eosinophilic cells, and some necrosis were found. In the attacked tissue some bundles of nerves were also seen. Benjamins ascribes all deviations to an allergic process, the primary cause of which was bilateral empyema.

VAN CREVELD, Amsterdam, Netherlands.

Surgery and Orthopedics

SURGERY OF CHILDHOOD. G. C. PENBERTHY, J. Michigan M. Soc. **35**:293 (May) 1936.

Penberthy writes briefly of the relationship of surgery of childhood to general surgery and general medicine. He also hopes for a clearer understanding of surgical problems of this age group. He takes up for special consideration appendicitis, intussusception, hernia, pyloric stenosis, empyema, osteomyelitis and burns.

CAREY, Detroit.

TOTAL REMOVAL OF A LUNG. R. MILNES WALKER, Brit. J. Surg. **24**:7 (July) 1936.

Total removal of a lung, or pneumonectomy, is done, first, for an inflammatory reaction, such as bronchiectasis or multiple abscesses, and second, for a new growth. It differs somewhat from lobectomy in that in lobectomy the remaining portion

of the lung still occupies the pleural cavity on that side, whereas in pneumonectomy there is a need for the obliteration of this cavity. A preliminary pneumothorax from ten to twelve days before the operation is of considerable importance, while just prior to operation postural drainage is carried out.

Walker summarizes the cases of total pneumonectomy to date, of which there are forty-four. The mortality rate was 45 per cent. Deaths following pneumonectomy are more frequent in the new growth class than in the inflammatory group. The death rate is greater in the older age group, and death has been found to be due to hemorrhage, shock, mediastinal infection, pneumonia and septicemia.

SUMMERFELDT, Toronto, Canada.

CLUBHANDS AND CLUBFEET ASSOCIATED WITH AMYOTROPHIC ABNORMALITIES IN THE LEGS AND ARMS. A. THOMAS and G. HUC, Rev. neurol. **64**:918 (Dec.) 1935.

An 11 year old boy presented these deformities at birth, with no progressive changes. Extensive neurologic examination revealed paresis or paralysis of the peroneal, gastrocnemius and quadriceps femoris muscles, while the arms presented typical Duchenne-Erb palsy. There were contractures of the antagonist muscles.

The authors consider this not so-called clubhand and clubfoot but the end-result of an intra-uterine infection with a superimposed traumatic or birth paralysis of the upper arms.

DAFFINEE, Boston.

A METHOD OF CONTINUOUS AND PROGRESSIVE TRACTION IN FRACTURES ABOUT THE ELBOW. JACQUES LEVEUF and HENRI GODARD, Rev. d'orthop. **23**:619 (Nov.) 1936.

The authors report on the use of the Kirschner wire extension in supracondylar and intra-articular fractures at the elbow. The forearm is encased in a splint up to the elbow, with the wire passed through the distal fragment. The arm is slung up by overhead traction, lifting through the Kirschner wire. The forearm is pulled across the body by traction attached to the splint, and countertraction is applied to the upper arm by a sling passed around the arm and weights pulling against the forearm pull. The forearm is held at an angle of approximately 80 degrees with the upper arm.

RYAN, Vancouver, Canada.

PERIDURAL (EPIDURAL) ANESTHESIA IN CHILDREN, WITH SPECIAL REFERENCE TO CYSTOSCOPY. R. SIEVERS, Arch. f. klin. Chir. **185**:359 (June) 1936.

Sievers considers the epidural use of procaine hydrochloride as the ideal method of producing anesthesia for cystoscopy in a child. Its chief advantage over general anesthesia is that it does not interfere with renal function. With care, there is no danger of injecting the drug intrathecally. The work of other surgeons is discussed with reference to their use of epidural anesthesia for general abdominal operations. The author describes twenty-one general operations of his own, in only fifteen of which the anesthesia was satisfactory. With forty of forty-two cystoscopies, satisfactory anesthesia was obtained.

DAFFINEE, Boston.

SKULL FRACTURES IN INFANTS. E. SCHIFF, Ztschr. f. Kinderh. **57**:654 (Feb. 26) 1936.

Skull fractures in infants are not as uncommon as would be expected from a consideration of the anatomy of the infantile skull and from clinical examination of infants who have suffered skull injuries. Three cases of skull fracture are reported and illustrated with x-ray pictures. In one case, in which the fracture resulted from a fall down six stone steps, the patient showed definite signs of cerebral injury. In each of the other two cases, in which the fractures resulted,

respectively, from a fall from the table to the floor and from a fall from the mother's arm to a carpeted floor, the only positive clinical finding was a small hematoma.

No recommendations regarding duration of treatment or of observation are made.

SIEMSEN, Chicago.

Teeth and Dentistry

CHILDREN'S TEETH IN RELATION TO PEDIATRIC PRACTICE. J. B. STONE, South. M. J. **29**:731 (July) 1936.

Dental hypoplasia and caries can be definitely influenced by diet, and the consumption of a diet containing liberal amounts of dairy products, eggs, bulky vegetables, fruits and cod liver oil is effective in the prevention and arrest of both hypoplasia and caries.

Stone observed a small group of cases under conditions prevailing in private practice.

Children with a history of breast feeding for from six to twelve months showed as high an incidence of caries as did those breast fed only one month or less.

Children whose prescribed diet included the so-called essential foods and cod liver oil or its equivalent showed about as high an incidence of caries as those who were first observed after 4 years of age and whose feeding history suggested a less adequate type of diet.

It was found that in children of good socio-economic status, with good general nutrition, both the incidence and the extent of caries was less than in those of poor socio-economic status or with poor nutrition. This suggests to Stone that the formation and preservation of sound teeth is closely related to good care and to good general health.

With the cooperation of a competent dentist, by inclusion in the child's diet of those things known to have a favorable influence on the arrest of caries and by other measures that will make for the child's best general health, much can be done to prevent further progress of the destructive process.

SCHLUTZ, Chicago.

SOME ASPECTS OF JAW GROWTH. M. R. DRENNAN, South African M. J. **10**:765 (Nov. 28) 1936.

Drennan declares that both environmental and hereditary factors are important in bone growth. The influence of environment on the genes, or internal factors, is shown by the development of one eye instead of two in the fish embryo (Fundulus) grown in water containing lithium chloride. There is also a close association between the presence of toxins of syphilis and the occurrence of developmental defects, which does not involve any alteration of the genetic content of inheritance. However, the influence of heredity cannot be denied. This is shown in the experiments of Murray and Huxley in which a very small piece of the hindlimb bud of a chick, when grafted on the chorio-allantoic membrane, grew into a highly differentiated and very easily recognized femur. What is true of the femur must be true of the jaws, so that no one can gainsay the dominant part the genes play in their formation, whether that be normal or abnormal. Modifying factors, also based on hereditary influence, may be found in endocrine abnormalities —as seen in the Hapsburg jaw.

A review of some recent advances in connection with the chemistry of bone growth emphasises the need for sufficient lime and phosphorus in the diet of the growing person. Vitamins are necessary, too, but all that they can do is to enable the organism to make the best use of the available resources. Studies of the diet and of the soils of the United States and South Africa, showing a deficiency in their mineral contents, indicate that it is probable that the average child is born with very definite osseous and dental handicaps. Consequently, the first few months after birth are the most critical months of the child's existence, and on the

efficiency of the measures which are then taken to insure that a good foundation will be laid for the future growth of the jaws and teeth will depend to a great extent the future dental history of the infant. For once facial growth has been allowed to become defective, the mutilation is permanent. To protect the infant and child, as well as the pregnant and nursing woman, the calcium and phosphorus requirements must be supplied. Although sufficient intake of vitamins is important it cannot make up for deficiencies in the mineral intake.

GONCE, Madison, Wis.

A MALFORMATION AND AN ANOMALY OF THE TEETH. J. MERLE-BÉRAL, Rev. de stomatol. **38**:844 (Dec.) 1936.

Orthodontic interest in the two reports is limited to that of a dental malformation in a boy of 9 which arose from a trauma in the area of the deciduous incisor at the age of 2. The patient was presented because of retrognathism caused by an apparent lingual malposition of the permanent upper right central incisor. The blow had fractured the deciduous upper right lateral incisor and rotated mesiolabially the approximating central incisor. These teeth were shed, and their successors erupted without incident beyond that of the lingual position of the right central incisor. X-ray films reveal that the latter tooth is not malposed but has a root-crown angle of about 45 degrees.

NEWCOMB, Cleveland. [ANGLE ORTHODONTIST]

DENTITION OF THE FETUS. MOLA and BOLAFFE, Ann. di clin. odontoiatrica **10**:875 (Oct.) 1936.

The authors review the usual time of eruption of deciduous teeth and on the basis of their clinical and histopathologic examinations divide fetal teeth into two categories: those in which there is simply an anomalous time of eruption and those in which, together with the anomaly in time, there are pathologic manifestations in the peridental and other tissues. They cite and describe the teeth of a patient with congenital syphilis who had seven teeth at birth and hazard the hypothesis that fetal teeth represent atavism and that their eruption, in the majority of cases, is due to pathologic changes associated with hereditary predisposition.

NEWCOMB, Cleveland. [ANGLE ORTHODONTIST]

COMMENTS ON SCHOOL DENTAL WORK AND THE STATISTICS RELATING THERETO. I. JUNDELL, Acta pædiat. **19**:245, 1936.

Jundell criticizes sharply the present organization of official agencies for the care of the teeth of school children. The number of working hours of the dentists assigned to this service and the number of patients assigned to each dentist have been determined quite arbitrarily, because of complete lack of reliable statistics relating to the incidence of dental disease among Swedish children. Furthermore, accurate figures are not obtainable concerning the value of the work of the school dental clinics. Minimum requirements are postulated for obtaining the statistics necessary for reorganization of this branch of the public health service.

MCCUNE, New York.

EXPERIENCES AND ACCOMPLISHMENTS IN THE SCHOOL DENTAL SERVICE AT DJURSHOLM (1931-1936). W. BERLIN, Acta pædiat. **19**:268, 1936.

In addition to cursory remarks relating to the technical aspects of the routine care of teeth of children, Berlin submits evidence for the conclusion that periodic examination of the teeth and regular treatment of minor defects lead to a manifest decrease in the occurrence of dental caries in school children.

MCCUNE, New York.

Miscellaneous

EFFECT OF INTRAVENOUS ADMINISTRATION OF PROTAMINE INSULIN. B. B. LONGWELL and A. RAVIN, Am. J. Physiol. **117**:453 (Nov.) 1936.

The action of protamine insulin after it has been injected intravenously does not differ significantly from that of regular insulin similarly injected.

NOURSE, Cleveland.

THE EUGENIC OUTLOOK IN PREVENTIVE MEDICINE. HORDER, Bull. New York Acad. Med. **12**:425 (July) 1936.

This is a philosophic yet practical discussion on eugenics delivered as the annual Herman Michael Biggs Memorial Lecture before the New York Academy of Medicine by Lord Horder, of London, England, on a recent visit to this country.

JAHR, Omaha.

COMMON ERRORS IN PEDIATRIC PRACTICE. J. GARLAND, M. Clin. North America **21**:535 (March) 1935.

The following are Garland's five causes for diagnostic error in the approximate order of their frequency:

Carelessness, to which all persons are susceptible to a degree dependent on inherited characteristics and early training.

Lack of available knowledge, which is frequently excusable, but not if knowledge is below a varying moderate level.

Lack of an innate or painstakingly acquired ability to draw on and correctly interpret the knowledge which one has.

Lack of accessory diagnostic facilities.

The unpredictable human factors represented in the patient, his heredity and the influences of his environment—factors which make him react in his own way to the conditions which are imposed on him.

Garland discussed these various sources of error in relation to certain specific conditions in childhood in which mistakes in diagnosis are frequently made.

EUGENE SMITH, Ogden, Utah.

A SIMPLE METHOD OF OXYGEN ANALYSIS FOR USE IN OXYGEN TENT THERAPY. J. E. F. RISEMAN and G. LESNICK, New England J. Med. **215**:65 (July 9) 1936.

An instrument for determining the concentration of oxygen within an oxygen tent is described. The directions for use are simple enough so that the apparatus can be used efficiently by a nurse or an attendant without previous instruction or experience. The method yields results which are accurate within 2 per cent. Instructions and working diagrams are given so that the instrument can be built by any one handy with tools. The retail cost of the necessary parts is approximately $4.00.

In principle, the method consists of absorbing the oxygen from a known volume of gas and determining the residual volume. The oxygen is absorbed by means of copper gauze and an ammoniacal solution. The article is illustrated.

GENGENBACH, Denver.

A NOTE ON THE PHYSICAL EXAMINATION OF CHILDREN. F. C. MCDONALD, New England J. Med. **215**:189 (July 30) 1936.

McDonald outlines the method used in the pediatric teaching clinic at the Boston Floating Hospital. Starting with what he terms functional dynamics, i. e., all movements, all functions relating to sight, touch, taste, hearing or smell, the examination then includes, layer by layer, the whole body, beginning with the ectodermal protective layers (skin, hair, nails, mucous membranes and the like).

GENGENBACH, Denver.

A Case of Chronic Arsenic Poisoning in a Child Associated with Profound Anemia and Scleroderma. L. Mary Moench, New York State J. Med. **36**:1029 (July 15) 1936.

An Italian girl of 14 complained of exhaustion, weakness and occasional shooting pains in the arms, legs and abdomen. She was found to have a hyperchromic type of anemia together with scleroderma. The urine was found to contain 0.15 mg. of arsenic per liter. Treatment with sodium thiosulfate gave good results. The source of the arsenic poisoning is not given.

Aikman, Rochester, N. Y.

A New System of Child Adoption. M. D. Anastasia, Bol. Inst. internac. am. de protec. a la infancia **10**:413 (Jan.) 1937.

The Children's Code, adopted by an Act of Congress of April 6, 1934, contains a chapter which, by providing considerable facilities for obtaining real homes for neglected children, treats and solves with a humane spirit one of the most stirring and difficult problems of child neglect. Chapter XIII of the code, "On Adoption," is an act of great importance and significance, the ultimate reach of which nobody can appreciate. Adoption has been awarded with the modern concept which it has enjoyed in such countries as France and Italy, where it is considered as child protective. Thus have been removed the most serious obstacles that hindered the system's greater diffusion and practicability. The age limit of the adopter has been reduced, and even parents of legitimate children have been allowed to adopt orphaned and morally abandoned minors. The adopter has been vested with all the attributes of paternal authority. The new law brings about an important innovation in that it exacts ample proof of the fitness and moral conditions of the adopter. Finally, the irrevocable character which this act used to have has been transformed so as to endow the act with the flexibility necessary to the new system of adoption.

From the Author's Summary.

Scientific and Social Development of Pediatrics in Hungary as Seen by an Italian Pediatrician. G. de Toni, Lattante **7**:292 (June) 1936.

Professor de Toni of the University of Modena writes regarding the history of pediatrics in Hungary and describes the pediatric clinics at Budapest, Debreczen, Szegedin and Pecs.

Higgins, Boston.

The Problem of Maturity for School in the Field of Biology of the Child. Hans Hummel, Arch. f. Kinderh. **106**:129, 1935.

The assertion made by Koch that the increase in the height and weight of present day children as compared with those of earlier periods may be attributed to earlier maturity is confirmed for the city of Jena, although there are other evidences that this is not the sole explanation.

The significance of this fact in determination of readiness for school is discussed. It was found that children who were presented for admission to school before the usual age did not on the whole reach the average height and weight of those admitted at the usual time. Methods for determining a child's readiness for school on the basis of physical findings, mental and emotional characteristics and intelligence tests are discussed.

Crane, Washington, D. C.

Pharmacology and Pharmacodynamics of Childhood: X. Hypnotics. E. Kramár and T. Varga, Arch. f. Kinderh. **109**:7, 1936.

By mouth or by rectum, the hypnotic doses of phenobarbital sodium are approximately as follows: first half year, 60 mg.; second half year, 75 mg.; preschool age, 120 mg.; school age, 150 mg. There is a progressive decrease in the relative dose (with relation to body weight). In contrast to what is observed in experiments on

animals, a disproportion between age and weight does not affect the dosage. Various factors affect individual susceptibility and tolerance but not so much that the use of the usual doses involves any danger. Two thirds of the hypnotic dose suffices as a sedative. Cumulation is shown earlier in infants than in older children. Undesired side reactions have not been observed.

By mouth, the hypnotic doses of urethane—which is not very dependable and often causes gastric disturbances—are: first half year, 0.8 Gm.; second half year, 1.0 Gm.; preschool age, 1.9 Gm.; school age, 2.2 Gm. Small children seem to have a strikingly high tolerance for urethane. CRANE, Washington, D. C.

ROENTGENOGRAPHIC ESTIMATION OF AGE FOR MEDICOLEGAL PURPOSES. I. IZKOVITCH, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:249 (Sept.) 1936.

Since 1927 Izkovitch has employed roentgenography in determining the ages of eleven accused persons. Estimation of age by this method depends on the state of ossification of the epiphysial centers. Although the results of the examinations were not highly accurate, they were accepted by the courts as decisive evidence in determining the fate of the defendants. Problems which arose in connection with one patient led to the examination of a small series of seven control patients between 16 and 19 years of age: Significant differences which were related to age were found in the time of union of the apophysis of the ilium.

McCUNE, New York.

CORRECTION

In the article by Dr. Josef Warkany, "Estimation of Vitamin D in Blood Serum," in the October 1936 issue (AM. J. DIS. CHILD. **52**:831, 1936), two errors occurred: On page 833, in the fourth line of the second paragraph under "Method," "30 per cent" should have read "20 per cent." In tables 1, 2, 3, 6, 7, 8, 9, 10, 11 and 12, the heading "Vitamin D content of Rat's Serum" should have read "Vitamin D Content of Rabbit's Serum."

Society Transactions

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

Fifteenth Annual Meeting, Niagara Falls, Ontario, June 11-12, 1937

A. P. Hart, M.D., *President*

Pearl Summerfeldt, M.D., *Secretary-Treasurer*

First Session

Friday Morning, June 11

Presidential Address: Hobbies. Dr. A. P. Hart, Toronto.

Rôle of Heredity in the Practice of Pediatrics. Dr. W. L. Denney, London, Ontario.

The study of heredity as related to human disease cannot be pursued in the manner of Mendel. Rather it must be based largely on the family pedigree and on the observation of identical twins under similar and different environmental conditions. It is suggested that the mode of transmission might be studied first, and in what manner identical genes can be influenced by environment secondly. The principles of recessive and dominant characteristics are explained, and the explanation is amplified by citing cases of hereditary defects, such as hemophilia, color blindness, congenital osteoma, absence of permanent teeth, chronic nephritis and acute rheumatic fever. The familial occurrence of acute rheumatic fever is demonstrated in two pairs of identical twins. One pair had simultaneous attacks of polyarthritis at 8 years of age, while the other pair had growing pains at 6 years of age. The hereditary factor in blood grouping is discussed, especially as a means of parental identification.

What possible use can be made of this knowledge of hereditary transmission? The question naturally subdivides itself into two parts: First, to what extent can faulty genes be eliminated from a family tree? Second, given a set of already active defective genes, what can be done to minimize or prevent their effects? To answer the first question entails the necessity of investigating in each case the pedigree for at least three generations in order to determine whether the trait is simple mendelian or sex linked, and, if mendelian, whether it is dominant or recessive. If the trait is found to be dominant mendelian, the answer is simple: The persons affected should not marry or at least should refrain from propagation. Persons in whom defective genes are already at work, one can still help through the ordinary processes of medicine and surgery.

Hereditary Osteochondrodystrophia Deformans. Dr. A. Wilmot Jacobsen, Buffalo, N. Y.

A boy aged 15 complained of a painful back for several years and showed progressive kyphosis. The conditions observed were: short stature in spite of apparently normal length of the extremities; an appearance as if the head had been forced down between the shoulders by pressure from above and the spine telescoped on itself; pronounced thoracic kyphosis and lordosis; marked pigeon breast; a rather apelike appearance due to the short neck and to the fact that the arms

reached nearly to the knees. Roentgen examination revealed the following abnormalities: flattening and broadening of the vertebral bodies, the vertical dimensions being reduced about 30 per cent; an irregularly wavy appearance of the superior and inferior borders; participation of the articular aspects of the ribs in the dysplasia, with flattening and broadening and with a slight indentation in the place of the normal articular tubercle; an expansion of the ribs, at the costochondral junction, giving a mixed cystic and sclerotic appearance; deformation of the head of the femur and shortening of the neck.

Then the information was obtained that other members of the family had the same affliction; that is, they were normal at birth, and kyphosis developed during childhood. Hence 3 children who were first cousins to the patient were brought in for roentgen examination. The eldest, a boy of 7½ years, showed definite changes of shape in the vertebral bodies; his brother, aged 3½, showed similar but less marked deformities of the vertebrae, while the sister, aged 2, had perfectly normal vertebrae. The grandfather of these children was located, and a roentgen examination revealed findings similar to those already described.

The condition is a hereditary defect in the normal process of conversion of cartilage into bone. The result is widespread deformity of bones, very marked in some persons, relatively slight in others. The most vulnerable part seems to be the spine, which is practically always involved. This is true not only of this family, in which kyphosis is an obvious defect in all affected members, but also of those families whose cases have already been recorded in the literature. While the clinical types are numerous and various, fundamentally they appear to be the same, and doubtless they are related to achondroplastic dwarfism.

Although Morquio is usually credited with the first description of the disease, published in 1929, as early as 1908 cases were reported which appear to belong to this group. The etiology is unknown, but the hereditary nature of the defect is recognized. It is clear that osteochondrodystrophia deformans is transmitted as a mendelian factor, recessive in the male. The disease may be transmitted through either the male or the female, but only males are affected. In this family, in every instance except one it was transmitted by the female, and every female who had offspring transmitted it to some of them. The only affected male who had children had (fortunately for the purposes of this investigation) a large family. None of his children had the disease, but both of his married daughters have male children who are affected. This is the type of heredity which is seen in red-green color blindness and in hemophilia. This is contrary to the statement of Shelling that the hereditary nature of the condition is probably determined, as in achondroplastic dwarfism, by a dominant mendelian factor.

FAMILIAL MULTILOCULAR CYSTIC DISEASE OF THE JAWS. DR. R. R. MACGREGOR and DR. W. A. JONES (by invitation), Kingston, Ontario.

These cases were first described by one of us (W. A. J.) at the meeting of the Radiological Society of North America at St. Louis, Dec. 1, 1931.

The condition is apparently one of multiple dentigerous cysts occurring throughout both the upper and the lower jaw and accompanied by a chronic hyperplastic disorder of the cervical lymph glands of the submaxillary regions.

The condition presents itself toward the end of the second year of life and is accompanied by bilateral painless swelling of both the upper and the lower jaw. The submaxillary lymph glands are enlarged. Roentgenograms and photographs of 3 children in the same family are shown, also roentgenograms and photographs in a similar case in a boy belonging to another family, with a genetic chart, showing the descent of the anomaly through 5 generations.

DISCUSSION OF PAPERS READ BY DRS. W. L. DENNEY, A. WILMOT JACOBSEN, AND R. R. MACGREGOR AND W. A. JONES

DR. A. P. HART, Toronto: I do not think there is any person practicing pediatrics who does not recognize the importance of heredity as a factor in life. Pediatricians have difficulty with the psychologists, who feel that too little emphasis is placed on it.

Dr. W. L. Denney, London, Ontario: These cases might very well be compared to Niagara Falls—one of the wonders of the world. While they are extremely interesting from the genetic point of view, they are not very helpful to one. The trend of disease is so marked in the population, and so few data are gathered—one has almost none. Medical students are not interested in genetics. I feel that there are a great many cases in which family trees and pedigrees could be recorded—pedigrees which do not merit a paper, but if records were made, there would be a nucleus on which a study related to pediatrics could be based.

Comparative Value of Spinach and Tomatoes in the Child's Diet. Dr. Frederick F. Tisdall, Dr. T. G. H. Drake, Dr. P. Summerfeldt and Dr. S. H. Jackson, Toronto.

Spinach has long been regarded not only by the general population but by physicians as particularly valuable in the diet of infants and children. This belief has been based largely on the high iron, calcium and vitamin content of spinach in the raw state. To obtain further information a study was made of the nutritional value of spinach as prepared for consumption, and for comparison similar studies were made on the almost universally available canned tomato.

The total iron content of cooked spinach is more than three times that of canned tomatoes. However, the amount of soluble iron, which is apparently the amount available for nutritional purposes, is approximately the same in both vegetables. Biologic determination of the hemoglobin-regenerating power of cooked spinach and tomatoes on anemic rats showed these vegetables to be of approximately equal value as sources of iron for the cure of nutritional anemia. The calcium content of cooked spinach is approximately twenty times that of canned tomatoes. However, when animals fed a diet low in calcium were given in addition cooked spinach or cooked tomatoes, it was found that the spinach actually tended to produce a negative calcium balance. On the other hand, the retention of the calcium in cooked tomatoes was excellent.

The vitamin A content of cooked spinach is approximately four times as great as that of canned tomatoes. The vitamin B_1 content of cooked spinach is approximately one-half that of cooked tomatoes. The vitamin C content of cooked spinach is less than one-quarter that of canned tomatoes. The vitamin D content of cooked spinach and canned tomatoes is negligible, as several hundred servings of either would be required to furnish the amount of vitamin D in 1 teaspoonful of cod liver oil.

A very appreciable loss of many of the food elements of spinach may occur in discarding the cooking water, even when the cooking is carried out under ideal home conditions. If these conditions are not observed, the loss may be greatly accentuated. On the other hand, no water is discarded in the preparation of tomatoes for consumption.

The results obtained indicate that the nutritional value of spinach has been markedly overrated. On the other hand, the nutritional value of canned tomatoes merits their more frequent employment in the diets of infants and children.

Trichophytobezoar: Report of a Case. Dr. George A. Campbell, Ottawa.

The patient whose story I wish to record is now 17 years old. Her infancy was uneventful except for an abscess under her jaw while she was teething and diarrhea at 16 months. Her hair was unusually long. At the age of 2 years it extended several inches below her neck, and her mother noticed that the front hair was broken off and just touched the shoulders. At 5 years of age she had a bald spot on the left side of her scalp about 5 inches (12 cm.) in diameter.

Last October, during a routine health examination by the school health officer, a mass was discovered in the epigastrium, and the child was referred to her family physician, who sent her to the hospital, where she came under the care of Dr. Philippe Belanger, through whose courtesy I am permitted to make this presentation. Roentgen examination revealed an unusual condition in the stomach, and

it was decided, in view of the history, to do an exploratory gastrotomy. The trichophytobezoar was removed, and the child made an uneventful recovery.

From the age of 2½ years she was very constipated, and the mother frequently pulled out long strands of hair from the rectum. She was placed in a convent from the age of 5 to that of 10 years and is reported to have had frequent attacks of vomiting.

Her weight at the time of operation in November, was 102 pounds (46 Kg.); in January it was 112 pounds (51 Kg.), and in April, 117 pounds (53 Kg.).

She persists in swallowing hair and also eats strings. She is losing weight now, and it is likely that another bezoar will be discovered before long.

She is always hungry with a very precocious appetite and explains that when she is hungry she breaks her hair off, twists it around the end of her tongue and then swallows it. Her mother mentioned that she had temper tantrums.

EARLY RECOGNITION OF CARDIAC IMPAIRMENT. DR. GEORGE R. PIRIE, Toronto.

The chief factor in the quality of a heart sound is the amount of tone. This can be measured by the oscillograph. In normal hearts, the amounts of tone in the various sounds are constant. The ratio between amounts of tone is the same in the sounds at the apex as in those at the aortic base. Any deviation from normal in these ratios indicates that the myocardium is not functioning to its full capacity. Such a sign can be elicited before other methods of examination show any change.

Sometimes the electrocardiogram will show lowered voltage, which improves as the sounds improve.

DISCUSSION

DR. LEONARD PARSONS, Birmingham, England: If I may be allowed, I should like to thank Dr. Pirie for bringing this communication before the society and to say how entirely I agree with him that students should be taught these methods. I have working with me in Birmingham a Toronto graduate, Dr. Keith, who is extremely interested in this subject. If Dr. Pirie could just alter his graphs somewhat, a greater change in the first sound could be detected, and he could give a representation of what Dr. Keith has found. With the alteration in the first sound, that is, as this becomes diminished, there is found a change in the electrocardiogram, which consists of great increase in the conduction time. When the first sound disappears altogether, the conduction time is increased up to two tenths of a second. With careful observation of the first sound, one can state when the conduction time is prolonged.

DR. E. A. MORGAN, Toronto: I should like to ask Dr. Pirie whether he notices this difference of sounds in the new-born, and, if not, at what age should one first recognize this in a child?

DR. GEORGE R. PIRIE, Toronto: I am interested to hear what Dr. Parsons says about Dr. Keith and that something has accrued from his teaching over here. In regard to Dr. Morgan's question as to when this difference in sounds is first recognized, I do not know in respect to adults. It is inconceivable to me that a man whose heart is examined today and who is told that the organ is normal should die in two weeks' time of coronary thrombosis. I think that every physician should train his ears to hear any abnormal sound.

DR. A. WILMOT JACOBSEN, Buffalo, N. Y.: Textbooks mention the tick-tack cardiac rhythm of the newly born child, and I have always felt that there was more or less evening up of the two sounds.

DR. GEORGE R. PIRIE, Toronto: I think there is more volume in tack than in tick.

SUBACUTE BACTERIAL ENDOCARDITIS. DR. GEORGE E. SMITH, Toronto.

Subacute bacterial endocarditis is rare in children before 10 years of age. This is probably due to the fact that the infection is usually implanted on a valve damaged by rheumatic fever. As this disease is rarely seen in a child before the age of 3 or 4 years, and some time is necessary to damage the valve, it follows that one cannot expect to see subacute bacterial endocarditis before this time. In

a small percentage—about 10 per cent—of the cases the heart showed congenital defects. In the Hospital for Sick Children, Toronto, there were in ten years but 3 cases in which the condition was diagnosed. Acute bacterial endocarditis appeared to be more common, 11 cases being encountered in this period.

Subacute bacterial endocarditis is caused, in 90 per cent of all cases, by a nonvirulent strain of Streptococcus viridans. The condition usually lasts longer than from two and one-half to three months. The characteristics of the disease are fever of septic type, clubbing of the fingers in 50 per cent of the cases, enlargement of the spleen in 65 per cent, pallor due to secondary anemia, progressive change in the cardiac signs and symptoms due to infarcts in the lungs when the disease is on the right side and to emboli in the systemic system if the disease is on the left side. Blood cultures are positive in a high percentage of the cases. The result is usually fatal. Libman reports recovery of 3 per cent of the patients.

DYSTROPHY OF THE LIVER IN INFANCY AND CHILDHOOD. DR. S. SANES (by invitation) and DR. D. P. ARNOLD, Buffalo, N. Y.

"Dystrophy of the liver" seems to be the most acceptable designation for a toxic infection, degeneration and necrosis of the hepatic parenchyma. Theoretically, the extent of the damage in the liver ought to depend on the action of the toxin, including its intensity and tempo, and on the susceptibility of the liver cells. The primary pathologic change is degeneration and necrosis of parenchymal cells. Reactive inflammation and autolysis remove débris. Then dilatation of sinusoids occurs. Finally, sinusoids and lobules collapse, with increase of connective tissue and of bile ducts. Partially damaged and spared parts regenerate in nodules. With the pathogenic and pathologic features just outlined in mind, a working classification can be made which includes under the one heading "dystrophy of the liver" conditions that superficially appear dissimilar and unrelated.

Three cases in patients about 3, 8 and 11 years old, which illustrate the clinical and pathologic observations in early acute toxic dystrophy, subacute toxic dystrophy and chronically recurring toxic dystrophy, respectively, are presented.

THE PROBLEM OF THE SEVERELY DEAF CHILD. DR. D. E. STAUNTON WISHART, Toronto.

In this paper an attempt is made to bring together for the information and interest of the pediatrician the facts and ideas regarding deafness which may prove of help to him in his practice. There is a discussion of what causes deafness, how different types of deafness are recognized by the pediatrician, what he can do for and to prevent deafness and what research is being accomplished in the otologic world.

Childhood is rightly regarded as the most precarious period in life so far as the ears are concerned. Certain diseases of childhood—meningitis, measles, scarlet fever and influenza—are the most important causes of both middle ear and nerve deafness.

It is extremely important to recognize defective hearing at the earliest possible age. Every infant is born dumb, but later on, owing to the sense of hearing, the child acquires articulate language. It is during the earliest years of life that the child with defective hearing should have special attention paid to it so that the remnant of hearing which it has may be made use of to the greatest possible extent in its preschool education. The child does not learn to speak properly unless it has good hearing, and such ability to speak as it has may be lost or not maintained if a hearing defect develops.

The parents and teachers should be advised that every child who requires to be told a thing twice should be examined by an ear specialist. The trouble may not be from inattention; it may be due to deafness.

Educational authorities are discovering that the handicap of deafness segregates the deaf child from the normal child and makes him less fit to develop into a

helpful citizen in his adult years. Cooperation between the pediatrician and the otologist is essential.

DISCUSSION

Dr. Alan Brown, Toronto: It is rather amazing to me that an otolaryngologist should get up before a group of pediatricians and tell them that they do not pay enough attention to deafness in children. Twenty-five years ago I could not find an otologist that could determine even whether or not an infant's drum was inflamed. It is only within the last fifteen years that otologists have condescended to use the auroscope. I think the average well trained pediatrician has probably forgotten more about babies' ears than the otolaryngologist will ever know. Apart from this, the reports were most instructive.

Dr. Haddon Keith, Montreal: For me Dr. Wishart's paper has been very timely. I have been presented with several cases recently in which parents have asked if their child was mentally retarded or deaf. I have one boy in mind—it was two or three years before I could make up my mind about him. At what age should one be able to recognize congenital deafness? At what age should one expect the otologist to give a measure of the amount of deafness in a child?

Dr. D. P. Arnold, Buffalo, N. Y.: I had somewhat the same opinion as Dr. Brown. Dr. Wishart said that in every case acute otitis should be taken care of. Apparently Dr. Alan Brown had the same reaction as I did concerning the acutely involved ears. I had thought the pediatrician knew as much about acutely inflamed ears and when they should be opened, but when it comes to chronically diseased ears, I must confess that I refer the patient to the otologist.

Dr. Haddon Keith, Montreal: Dr. Wishart said nothing about lip reading. At the New York Lip-Reading Institute they have some very wonderful demonstrations of lip reading.

Dr. George E. Smith, Toronto: Is the electric audiometer applicable to classes in schools? Is it used, and with what results?

Dr. B. Hannah, Toronto: Dr. Wishart spoke of the prevalence of acquired deafness, which the members of this society are much interested in, and said it was frequent following measles and scarlet fever. In the last fifteen years, what is the relative prevalence of measles and scarlet fever as related to deafness, in comparison with the previous fifteen years? I should like to draw attention to this in the training of medical students and pediatricians.

Dr. D. P. Arnold, Buffalo, N. Y.: Following acute otitis, how often should a child have his ears "blown out"? I have heard ear, nose and throat specialists speak of this a number of times.

Dr. E. A. Morgan, Toronto: Speaking of deafness following scarlet fever and measles, how often does one see nerve deafness following these diseases? Nerve deafness must be produced by toxemia and damage to perception. Could otitis media from these diseases have the same effect as otitis media from any nose and throat infection? How often does nerve deafness follow these diseases?

Dr. D. E. Staunton Wishart, Toronto: I infer from Dr. Brown's remarks that there has been a change for the better in the last twenty-five years in the ear, nose and throat specialists, in that they have followed the pediatricians in being wise enough to use any device that will enable them to see an ear better. Dr. Keith asked me at what age a pediatrician could recognize deafness and at what age an otologist could make a diagnosis of deafness in a child. I don't think Dr. Keith's questions can be answered dogmatically. Every case is a law unto itself. There are some children with whom it has been possible to make a definite diagnosis at the age of 4, but in testing for deafness one depends much on the subjective response of the child, and one has to have a child who is both intelligent and cooperative, who has confidence in the examiner and who will respond intelligently. Although these questions cannot be answered dogmatically, some attempt should be made by the pediatrician to appreciate that the child has a degree of deafness. The otologist should be able to give the parents the prognosis.

Dr. Arnold asked how often the eustachian tubes should be "blown out." I should say, just as seldom as possible. Occasionally I get a shock when I work on the ears and find that a child is hopelessly deaf and that there is no use "blowing out" the tubes—the child has nerve deafness; to my surprise, I have on occasion "blown out" the tubes and obtained some return of function. I omitted lip reading because this is advisable only for the child who is hopelessly deaf or a deaf-mute. But this problem of hearing is vitally linked with the education of the child. Every child is born dumb and remains dumb unless he hears some sound to copy. What one has to consider in every child who is deaf is how to utilize to the best advantage the amount of hearing he has, and that is why I suggest the use of the electric hearing device, so that the child may hear as much of the school teaching as he can from hearing the voices around him. Dr. Smith asked if the audiometer is used in schools. Generally it is not. Its value is in helping school authorities to pick up the children who should be sent to the otologist for examination—those children who have a certain degree of deafness.

Dr. Hannah asked me a question which I think he knows I cannot answer—regarding statistics of the incidence of measles and scarlet fever. In my paper I have stressed the fact that in England a great deal of work is done for the deaf. A deaf person can receive information on deafness anywhere in England, and he is prevented from being exploited. Some research is going on in the United States, but in Canada there is none. Accurate statistics have been given in both England and Scotland, and they have shown that in recent years the amount of acquired deafness in schools has become a great deal less than twenty years ago. Greater attention is paid to the health of the child by the pediatrician.

PROLACTIN: ITS EFFECT ON SECRETION OF BREAST MILK. DR. JOHN R. ROSS and DR. ALAN BROWN, Toronto.

Prolactin (the lactation-stimulating principle of the anterior lobe of the pituitary gland) was administered intramuscularly to mothers whose daily secretion of breast milk on the fifth and sixth days was less than 400 cc. The injections were given twice daily over a two day period. One group of patients received a total of 400 units, while the second group received a total of 1,000 units. A control group of patients received intramuscular injections of physiologic solution of sodium chloride.

In the higher concentration prolactin appeared to increase slightly the secretion of breast milk during the remainder of the stay in the hospital. Of much more significance, however, was the fact that 7 of 11 patients receiving this higher concentration whom it was possible to follow after discharge from the hospital nursed their infants completely, while, of 8 patients receiving the lower concentration who were followed, only 2 were able to nurse their infants completely. Of the 8 controls who received physiologic solution of sodium chloride and were followed, only 1 nursed her infant completely.

The prolactin administered apparently had no effect on the fat, protein or ash content of the breast milk secreted.

The galactagog effect obtained justifies further investigation of the value of this product.

The urinary excretion of estrogen in these cases was within the range found during the normal menstrual cycle.

DISCUSSION

DR. A. P. HART, Toronto: Apparently Dr. Ross has demonstrated that the large unitage is of benefit, but a great disadvantage is the accompanying reaction. If he could try a larger dosage in the more dilute form, it might be very successful.

DR. ALAN BROWN, Toronto: About twenty years ago, Abraham Jacobi made this statement: "Every woman, even the flower of fashion, can nurse her child. There is no such thing as absence of secretion." I think this is an important clinical factor. A number of years ago, before the collection of breast milk was adopted in Toronto, wet nurses were employed. There was one who started off with her

own baby and finally nursed 9 babies every twenty-four hours. In certain areas in Africa, where the natives are unable to get the type of food they require, the mothers nurse their children until these are 3 or 4 years of age; they also take on the nursing of babies of mothers who die. There is no question that there is very much less breast feeding today that there was from fifteen to twenty years ago. There are many factors in modern life contributing to this. The secretion of breast milk and the secretion of cow's milk are identical, but the situations are different. The cow secretes its milk under a shady tree, surrounded with green grass and calm water. The average young woman endeavors to secrete breast milk listening to the radio. This work done by Dr. Ross is interesting. The idea of seeing if it is possible to find some method of overcoming the prevention of natural feeding of babies is a good one. I think the results are rather disappointing.

Dr. Frederick F. Tisdall, Toronto: I agree with Dr. Brown that from the clinical standpoint the results are disappointing. But from the standpoint of the investigator they are stimulating. It has been definitely shown that it is possible to increase breast milk by methods such as this.

Dr. S. Graham Ross, Montreal: Has work been done on the effect of this lactogenic product on the breast which is not secreting milk?

Dr. John R. Ross, Toronto: I do not believe that the lactogenic substance mentioned has been shown to stimulate a breast that is not secreting. The animals used were all in the puerperal state, and I think that, it would not be possible to produce secretion in a nonparous animal without previous treatment with estrogen and progesterone.

Chemotherapy in the Treatment of Streptococcic Infections of the Lung, Pleura and Chest Wall (Sulfanilamide). Dr. Alton Goldbloom and Dr. H. C. Ballon (by invitation), Montreal.

Following the work of Colebrook, Long and Bliss, and others, on the effect of sulfanilamide and its derivatives on infections due to hemolytic streptococci, we report our experiences in 3 cases involving infections of the lung, pleura and chest wall.

The first case was that of a child 11 years old. She had been suffering from complications of scarlet fever in the form of suppurative cervical adenitis and cellulitis, lasting for a period of sixteen months, with ulceration, collar fashion, about the entire neck, culminating in periostitis involving the clavicle and three ribs on the left side, with subpectoral and subtrapezial abscess. The condition rapidly subsided on the administration of sulfanilamide. The sinuses healed, and the child gained 25 pounds (11 Kg.) in a short period.

The second case was that of a child 10 years old who had unresolved pneumonia with high fever, extreme intoxication and loculated collections of fluid in the chest. Hemolytic streptococci were shown on culture. A derivative of sulfanilamide was administered at a time when the child seemed almost moribund. The use of this drug was followed by rapid defervescence and less rapid resolution of the pneumonia.

The third case was that of a small boy aged 4 years with an acute pneumonic process, followed rapidly by a purulent pleural effusion, which on culture yielded hemolytic streptococci. No operation was performed beyond removal of a few cubic centimeters of thoracic fluid for diagnosis. Complete resolution followed administration of sulfanilamide and one of its derivatives.

In these three cases the new treatment met with outstanding success in conditions which hitherto had been far less amenable to simple treatment.

DISCUSSION

Dr. A. Wilmot Jacobsen, Buffalo: I might add to the remarks that, of a group of 5 patients with hemolytic streptococcic empyema at the Children's Hospital, Buffalo, 4 were cured with sulfanilamide. In one case the drug was given

intravenously, and there was prompt improvement. I feel that it is highly advisable to give sodium bicarbonate with each dose, which eliminates the possibility of acidosis.

Second Session

Saturday Morning, June 12

ACUTE SALICYLATE POISONING. DR. L. M. LINDSAY, Montreal.

Numerous cases of acute salicylate poisoning have been reported in medical journals.

Sodium salicylate poisoning may result from moderate doses in persons who have low tolerance for the drug.

Aspirin (acetylsalicylic acid) has often been taken with suicidal intent. Five hundred grains (32 Gm.) is the average lethal dose. Rarely aspirin may cause unexpected death as a result of anaphylaxis.

Methyl salicylate (oil of wintergreen) is the most poisonous of all when taken internally. Usually in such cases it is taken inadvertently by small children, who as a rule succumb within forty-eight hours. The case histories of 2 such victims are reported. One at autopsy showed subserous and parenchymal hemorrhages, which are characteristic of salicylate poisoning, the result of general vascular damage. The similarity of the picture to that of diabetic coma is emphasized and discussed.

So-called salicyl dyspnea is due to irritation of the respiratory center of the brain. Acidosis results from depression of renal function, due to tubular damage by the poison.

Coma and convulsions are due to cerebral and meningeal congestion and hemorrhages.

Treatment demands elimination of the poison by emesis, gastric lavage, drainage of cerebrospinal fluid and stimulation of the kidneys by intravenous injections of dextrose in saline solution. Stimulants and sedatives are administered as indicated by the condition of the patient.

The prognosis is good in sodium salicylate and aspirin poisoning if prompt treatment is instituted, but treatment seems of little avail in stemming the fatal issue resulting from methyl salicylate poisoning.

DISCUSSION

DR. A. P. HART, Toronto: I am sure all are indebted to Dr. Lindsay for bringing this subject to their attention, particularly the similarity of this type of poisoning to diabetic acidosis. One could easily make a mistake if the blood sugar or carbon dioxide could not be readily determined.

DR. H. B. CUSHING, Montreal: I had the opportunity of observing these cases reported by Dr. Lindsay and was much interested. Oil of wintergreen is widely used, and bottles of it which are not labeled poison are in many households. It is not generally recognized that a small quantity of this substance is invariably fatal. In one of the cases reported the victim swallowed a small amount. He was taken immediately to a large hospital in Montreal. His parents were assured that there was no danger, and the child was sent home. After some hours he vomited and was taken to another hospital and went home again. He was finally taken to the Children's Memorial Hospital, and his condition was found to be absolutely hopeless. It is important that oil of wintergreen be recognized as a dangerous substance to have in the house, and any swallowing of even a small amount should be regarded as a very serious happening.

DR. D. P. ARNOLD, Buffalo: I attended a child 9 months old who had taken a small amount of oil of wintergreen from a bottle. Two doctors were called in. The child showed no symptoms at first, but died in a couple of days. It is important to recognize that there are no symptoms for the first hour or two. One

always hopes that perhaps the child has not taken a sufficient amount to do it harm, and antidotes are not used. One must recognize the danger of this attitude.

DR. P. W. BEAVEN, Rochester, N. Y.: About two months ago I saw a child who had rheumatism over a period of a month; there was no history of ingestion of oil of wintergreen, but this had been applied to the joints. The child showed deep hyperpnea and fever. She died within forty-eight hours. The observations at autopsy were typical of salicylate poisoning. This is unusual since there was no history of ingestion of salicylate.

DR. L. M. LINDSAY, Montreal: Dr. Beaven's point is very interesting. A few years ago Brown and Scott proved by a series of experiments that methyl salicylate could be absorbed by the skin, more especially when applied hot or when rubbed in. While this form of poisoning must be rare, it should not be forgotten, and it should warn against using oil of wintergreen externally for more than a few days at a time.

MATURATION OF THE RED CELL. DR. LEONARD G. PARSONS, Birmingham, England.

Views on the maturation of the red cell, elaborated as the result of experimental and clinical work on anemia carried out at the Children's Hospital, Birmingham, are put forward. The scheme of maturation suggested differs from that commonly accepted (for example, Witts') in two observations: 1. Three factors—anoxemia, vitamin C and thyroxin—act throughout the entire range of maturation and are not restricted to the stage of maturation from normoblast to erythrocyte. 2. Apart from the microcytosis of acholuric jaundice, true microcytosis connotes deficiency in hemoglobin, usually the result of deficiency in iron.

In anoxemia the reaction of the bone marrow is usually normocytic but may be macrocytic, and examples of such macrocytosis (as shown by Price-Jones curves) have been observed in the following conditions of anoxemia: sudden collapse in idiopathic hypertrophy of the heart, severe hemorrhage, severe hemoptysis (acute erythroblastic anemia of the Lederer type) following a severe crisis in acholuric jaundice, and acute leukemia.

Anemia is not always present in scurvy but was observed in 7 of 14 cases. It is usually orthochromic and normocytic but may be macrocytic; it is cured by administration of vitamin C in the form of orange juice or cevitamic acid.

Thyroxin acts in a way similar to that of the other two factors. Of 9 cretins, all were anemic. The anemia was normocytic or macrocytic and was cured by administration of thyroid, with, in one case only, addition of iron. Roentgenograms of the bones showed dense transverse lines in the diaphysis, thickened cortices and small medullary centers, the latter condition being due to aplasia of the bone marrow; these appearances became normal under treatment.

True microcytosis, with the exception of that in acholuric jaundice, has been found only when there has been deficiency of hemoglobin. In such conditions the bone marrow is hyperplastic, not hypoplastic or aplastic, and produces many small cells, so that the reparatory action of hemoglobin can be used to greater advantage than if it were present in a smaller number of normal or large-sized cells. The factors required for the synthesis of hemoglobin are iron, copper and possibly other elements, such as vanadium, cobalt, nickel and calcium, and the pyrrol ring. Proof that such hyperplastic microcytosis occurs is based on:

1. Experimental evidence: Rats fed on a diet slightly deficient in iron showed normal hemoglobin but polycythemia and microcytosis, and administration of adequate amounts of iron produced normal-sized cells and a normal cell count.

2. Clinical evidence: Sometimes during cure of nutritional anemia by iron, Hagen's phenomenon occurred; that is, before the hemoglobin returned completely to normal, the red cell count reached 6,000,000 per cubic centimeter or more, whereas when the hemoglobin reached normality the red cell count also became normal. Examples of the cure of nutritional anemia by administration of copper and also by that of bile pigments, which contain the pyrrol ring, are also cited.

DISCUSSION

DR. C. E. SNELLING, Toronto: I listened to Dr. Parson's paper with great pleasure and interest. The presentation was instructive. Many points which he illustrated will help to explain some of the cases which my associates and I have observed. There are certain types of blood change that I am going to ask him to explain. In new-born babies the mean diameter of the red cells is larger than the accepted normal. I suppose it is purely a matter of anoxemia. The cell size decreases gradually up to 6 months of age, when the mean diameter is less than normal. Also, occasionally in celiac disease one sees macrocytic anemia, which is sometimes similar to what one sees in pernicious anemia. In scurvy some findings are not constant. One does not always see improvement in the anemia on giving vitamin C. Some patients require transfusion of blood as an additional measure. I was interested in the discussion of cretinism as a cause of anemia. The lack of bone marrow space may be similar to the cause of anemia in premature babies. Sufficient space is needed for the red blood cells to form.

DR. P. SUMMERFELDT, Toronto: I was interested in what Dr. Parsons had to say about rats fed on a subminimal amount of iron. I should like to ask if the results can be applied to man, especially to new-born babies whose mothers have had a low iron diet?

DR. LEONARD G. PARSONS, Birmingham, England: In answer to Dr. Snelling's question, I think that in the new-born the probability is that the cells become smaller at 6 months, indicating deficiency in iron if the infant has had no infection, but this seldom is the case. In celiac disease macrocytic anemia may be due to two deficiencies: There may be a lack of the intrinsic factor, or there may be a lack of the extrinsic factor. With regard to scurvy, I think it is possible that in some cases deficiency of vitamin C may be combined with deficiency of iron. Patients whose anemia clears up with administration of vitamin C do not require iron.

Dr. Summerfeldt's question enters a big field. I feel very definitely—although it has not been proved yet—that hypochromic anemia occurs in babies as a result of iron deficiency in the mother's diet. My colleague, Dr. Gidden, gave iron to mothers, and the children showed much better hemoglobin. I think there is no doubt that hypochromic anemia may develop in the new-born infant as a result of a deficient diet in the case of the mother.

OSTEOMYELITIS OF THE SUPERIOR MAXILLA IN THE NEW-BORN INFANT. DR. ALTON GOLDBLOOM and DR. H. L. BACAL (by invitation), Montreal.

Osteomyelitis of the maxilla in the new-born infant is rare, yet a striking uniform clinical picture of an inflammatory and suppurative process occurs, which results in necrosis and sequestration of the maxilla in one or all of its surfaces.

Wilensky gives a comprehensive review of the clinical course, pathogenesis and treatment of the disease. He finds that the organism most commonly found in this condition is Staphylococcus aureus. It is his impression that the sources of the infection are: (1) the vaginal canal of the mother; (2) the fingers of the accoucheur or of the nurse; (3) the nipples and breasts of the mother, and (4) the fingers or apparatus used in cleansing the baby's mouth after birth.

The clinical course is clearcut, with classic signs so typical that one case is almost an exact replica of any other.

Any new-born infant presenting a unilateral swelling of the face with fever should be suspected of suffering from this condition. When a unilateral nasal discharge develops in addition, the diagnosis is complete.

The prognosis is generally good. Children surviving the first onslaught of the infection usually recover, although convalescence may be greatly prolonged and complicated by frequent sequestrations of dental buds or bits of the maxillary bone.

Another case is added to those recorded in the literature—that of a white boy 3 weeks of age with classic signs and symptoms of osteomyelitis of the superior maxilla.

DISCUSSION

DR. ALAN BROWN, Toronto: Approximately fifteen years ago I observed a case that was almost a duplicate of Dr. Bacal's. In that case the child, of course, became pitiably scarred, though treated medically in the same fashion. What I am concerned about in the present case is whether Dr. Bacal thinks there was any benefit from the use of staphylococcus toxoid, whether he obtained the titer of the staphylococcus in the child's serum, and whether he noticed that the toxoid had any effect? Recently Dr. Robertson reviewed the cases of osteomyelitis that have been encountered in the Toronto Children's Hospital during the last ten years —in 96 per cent Staphylococcus was the cause. Just recently an article from Boston was published in which it was reported that in most of the cases concerned the condition was due to Streptococcus and that Staphylococcus rarely produced a sequestrum. This is exactly opposite to our observation: Staphylococcus is the cause in all cases, and it is Staphylococcus that produces sequestrums. I have observed a case in which the condition was probably due to infection of the umbilical cord. My patient also had several abscesses of soft tissue in other parts of the body, with no other bone involvement.

DR. D. P. ARNOLD, Buffalo: How is it that the prognosis is so good in staphylococcic septicemia?

DR. H. L. BACAL, Montreal: We felt that the staphylococcus antitoxin was of no benefit in this child. We cultured an area and obtained Staph. aureus. There was no evidence of infection over the umbilical area. Regarding Dr. Arnold's question, in our cases the blood cultures were negative and the children had acquired immunity by then (2 weeks of age).

TREATMENT OF BRONCHIECTASIS IN CHILDREN. DR. GLADYS L. BOYD, Toronto.

The various therapeutic measures that may be used in the treatment of bronchiectasis are discussed. Approximately 200 children with bronchiectasis have been treated at the Hospital for Sick Children, Toronto, in the past ten years. In an attempt to estimate the relative value of each remedial measure, a special study was made of those patients who were first treated four years ago and are still under observation.

From this study it appears that there are few, if any, who cannot be helped by treatment and many who can be clinically cured. In those in whom the condition is more severe, recovery is slower and more difficult, and some become discouraged before the desired result is obtained. Surgical removal of the diseased lung offers the only cure that lasts. Lobectomy in skilled hands has become much easier and in selected cases gives brilliant results. In those in whom a major surgical operation is contraindicated or inadvisable, much help of lasting value is afforded by repeated bronchoscopic suctions, with postural drainage, or by collapse therapy, such as pneumothorax or phrenicotomy.

DISCUSSION

DR. A. H. SPOHN, Vancouver: Dr. Boyd should be complimented on her careful report of such a large number of cases. As sinus infections are so closely related to subsequent bronchiectasis, it is essential that careful treatment of all conditions of the upper respiratory tract should be carried on early and consistently. I think that suppurative discharge can be maintained from many antrums by constant lavage. I was interested in some cases of Dr. Chiari, of Vienna. He reported 14 cases of bronchiectasis in which the condition was treated successfully without extensive operative procedure. In all these cases bronchiectasis had been produced through occlusion of a division of the bronchial tree with caseous material, which had ruptured through from an adjacent tuberculous bronchial gland. The caseous material was skilfully removed through a bronchoscope, and recovery occurred subsequently. As 14 cases have been discovered by Dr. Chiari, working in the Hamburg clinic, it seems that it would be advisable to eliminate such cases before proceeding with extensive surgical treatment.

DR. T. CROSSAN CLARK, Hamilton: From 250 cases, you selected 100 to cite. What percentage of the 250 patients are still living?

DR. GLADYS L. BOYD, Toronto: All but 4 are still living; 3 died following bilateral lobectomy. I picked these 100 cases because in them there had been from four to five years between the time of treatment and now.

DERMATORRHEXIS: REPORT OF A CASE. DR. ALAN BROWN and DR. V. F. STOCK (by invitation), Toronto.

The patient was first seen by one of us (V. F. S.) in June 1933, when he was 10 years of age. The following were the chief complaints which his parents brought to our attention: 1. Since childhood, moderate or slight injury had always produced (*a*) a large hematoma, over which the skin sloughed off in two or three days, or (*b*) a widely gaping wound which suture did not retain. These wounds healed gradually, leaving large tissue paper-like scars. The regions in which these lesions occurred were the forehead, elbows, knees and shins. Owing to this condition he had been unable to play games. 2. His teeth became carious readily, and there was a tendency toward formation of apical abscesses. 3. He was loose jointed and double jointed. 4. The muscles of his legs were not as firm as one would expect them to be in an active boy.

Medical History.—Nothing abnormal was noted until the boy was approximately 18 months of age, when he commenced to walk. It was then observed that whenever he fell and bumped his head an injury of the type complained of occurred. At first he experienced difficulty in walking. His ankles were weak, and it was necessary for him to wear boots with ankle supports. As he grew older and played games, whenever he fell on his knees, shins or elbows the skin tore up like a flap, and healing occurred in the manner mentioned.

There was no family history of a similar condition.

Physical Examination.—At 10 years of age, this child was 52¼ inches (132.7 cm.) tall and weighed 64 pounds (29 Kg.). He was well nourished and appeared to be normally developed. On his forehead were numerous white scars. His left elbow and both knees were covered with thin parchment-like, raisin skin-like scars. Both shins were disfigured with numerous large scarified areas. The skin generally was loose and hyperelastic; that over the knee joints could be stretched to an abnormal degree. The texture appeared normal. The muscles seemed looser and less firm than one would expect for a boy of his age who had been quite active. All the joints appeared to be somewhat loose, and both thumbs could be hyperextended. There was a definite tendency toward flatfeet. The teeth contained a good many fillings. In other respects, physical examination showed no abnormalities and no congenital abnormalities were noted.

It was found that suturing was of little avail, as the wound always broke open, leaving a large granulating area, which gradually healed in. Adhesive strips served better in keeping the skin flaps approximated.

Additional investigations showed (1) the blood clotting and bleeding time normal, (2) the Wassermann reaction negative, (3) the blood calcium 10 mg. per hundred cubic centimeters, (4) the basal metabolism rate + 6, (5) the hemoglobin rate 85 per cent, red blood cells 4,000,000, the white blood cells 9,900 and the platelets normal.

This is the third report of such a case in the American literature, the first being that of N. Tobias (Danlos Syndrome Associated with Congenital Lipomatosis, *Arch. Dermat. & Syph.* **30**:540 (Oct.) 1934) and the second that of F. Ronchese (Dermatorrhexis with Dermatochalasis, *Am. J. Dis. Child.* **51**:1403 [June] 1936).

The most important features of the condition as observed in this case are, first, pronounced fragility of the skin and its blood vessels, with breaking, splitting and formation of a hematoma and pseudotumor subsequent to the slightest injury (dermatorrhexis-fragilitas cutis); second, more or less pronounced hyperlaxity and hyperelasticity of the skin (dermatochalasis-laxitas cutis), and, third, more or less pronounced hyperlaxity and hyperflexibility of the joints (arthrochalasis-laxitas articularis). These three factors complete the Ehlers-Danlos syndrome.

The biopsy, done by Dr. I. H. Erb, showed fragmentation and thinning out of the collagen fibers of the corium, diminution in the number of elastic fibers and flattening of the interpapillary digitations. It is suggested that the underlying cause of these changes is some congenital defect in the collagen fibers, which do not possess their normal tensile strength, thus allowing the skin to be stretched beyond its normal limit. The other changes are interpreted as secondary and of traumatic origin.

DISCUSSION

Dr. Roy W. Simpson, Toronto: Mr. Chairman, I should like to add another case almost identical with this one. The photographs of the legs showed almost identical raisin-like scars, and there was susceptibility to wounding. I saw this child again a few days ago. The father had counted 285 stitches being put in and then lost count. The boy is now 16 years of age. He shows extremely elastic skin and hyperextensibility of joints. He fell three or four years ago some 2 feet (61 cm.) and dislocated his left elbow; now he has a deformity of the left arm.

Value of Mapharsen in the Treatment of Congenital Syphilis. Dr. E. A. Morgan, Toronto.

The report consists of a statistical study of 40 cases in which treatment was by means of mapharsen, with a view to determining the value of the drug and particularly its effect on the Wassermann reaction.

The conclusions are: Mapharsen is a safe form of arsenic; it is easily administered; the reaction is mild and can be eliminated by careful attention to the dosage, and the effect on the Wassermann reaction is probably slightly greater than that obtained with other arsenical compounds previously used. The proper standard for treatment of children was established at 0.6 mg. per kilogram of body weight.

DISCUSSION

Dr. Alton Goldbloom, Montreal: Dr. Morgan's review does not give exact figures in the comparison with other arsenical preparations. I should like to know how mapharsen compares with acetarsone.

Dr. P. W. Beaven, Rochester, N. Y.: Do you combine mapharsen with anything else?

Dr. A. Wilmot Jacobsen, Buffalo, N. Y.: I should like to ask the same question as Dr. Goldbloom in regard to sulfarsphenamine given intramuscularly.

Dr. E. A. Morgan, Toronto: In answer to Dr. Goldbloom's question, I have no series showing the value of acetarsone. I am convinced that the ideal way to give arsenic is intravenously. Acetarsone is very good in small infants when one is unable to give arsenic intravenously. My associates and I still adhere to the latter route. In the early stage, the results are so good with intravenous treatment that I see no advantage in switching to another. In the clinic we have treated patients exactly the same way with arsenic and then with mercury. We don't combine mapharsen with bismuth. In answer to Dr. Jacobsen's question, we have no series of cases in which we treated the patients intramuscularly with sulfarsphenamine. We don't like to use intramuscular injections. Parents submit themselves to severe reactions, to pain and discomfort, but won't bring their children for this type of treatment. Regular and persistent treatment is one of the requisites for cure.

A Peculiar Case of Blindness. Dr. Roy W. Simpson, Toronto.

A child 3 years of age had the following symptoms: elevation of temperature for seven months, pains in the regions of the joints on and off for seven months, recurrent secondary anemia for seven months, blindness followed by proptosis, of sudden onset, for two and a half months, swellings under the scalp for one and a half months and a tumor mass in the abdomen for one week.

Autopsy showed neurocytoma of the right adrenal with secondary growths in the muscles of the iliac fossae and in the ovaries, the para-aortic glands, the pancreas and the skull, with particular invasion of the orbital plates of each eye.

NEUROBLASTOMA OF THE ADRENAL MEDULLA. DR. I. H. ERB, Toronto.

The material forming the basis of this paper was gleaned from the autopsy records of the Hospital for Sick Children, Toronto, during a fifteen year period, ending April 30, 1937. During this time, in a series of 3,443 consecutive autopsies, 13 cases of neuroblastoma of the adrenal medulla were encountered. A fourteenth case of neuroblastoma, clinically of the Hutchison type, verified by biopsy, is also included in the report, but, as autopsy was refused, it is impossible to state whether the tumor arose from the adrenal medulla or from some other part of the sympathetic nervous system. These cases all came under my personal observation.

As a basis of a better understanding of the origin of the neuroblastoma of the adrenal medulla, the embryology and histology of the adrenal medulla are discussed first. Then follows a brief review of the gradual development of knowledge of this peculiar tumor of infancy and childhood. Because of the wide variety of names by which the tumor is known, an attempt is made to clarify to some extent the more or less chaotic terminology.

The fourteen cases fall naturally into three main groups: (1) cases in which the adrenal tumor was encountered accidentally at autopsy; (2) cases of what is commonly known as the Pepper type, and (3) cases of what is commonly known as the Hutchison type.

Group 1 contains 4 cases, in none of which were any metastases shown. The oldest child in this group was a girl of 3 years. She died of meningitis following an automobile accident in which she sustained a fractured skull. In the left adrenal was found a tumor the size of a golf ball, showing numerous microscopic rosettes. Of the other 3 patients in this group, 2 were girls 6 months of age. One died of hydrocephalus; the other, of osteomyelitis. The third patient was a boy 12 months of age, who died of tuberculous meningitis. These 3 infants showed smaller medullary tumors, 2 in the left and 1 in the right adrenal.

Group 2 includes 4 cases of the Pepper type, that is, a type in which the metastases are largely to the liver, which may become enormously enlarged. The ages in this group were as follows: 6 weeks, 7 weeks, 11 weeks and 10 months, all under 1 year. In the case of the 10 month old infant, a boy, the primary tumor was on the left side, while in the other children, all girls, both adrenal medullas were involved.

Group 3 includes 6 cases of the Hutchison type. The children with this type are commonly older than those with the Pepper type, and metastases are common in the skull. These features were common to all 6 cases.

The youngest patient in group 3 was a 13 month old boy with a primary tumor in the left adrenal. The remaining patients were as follows: 2 boys, each 3 years old; 1 girl 3 years old; 1 girl 5 years old, and 1 boy 7 years old. In this group, the primary tumor was on the left side in 2, on the right side in 2, bilateral in 1 and undetermined in the patient in whose case autopsy was refused.

Microscopically, all the growths showed undifferentiated sympathicoblasts. In 7 cases, rosette arrangement was demonstrated in varying degrees. In only a single case were ganglion cells found.

No relationship between the side on which the primary growth was situated and the side on which cranial metastases developed, as suggested by Frew, could be demonstrated.

DISCUSSION OF PAPERS READ BY DRS. ROY W. SIMPSON AND I. H. ERB

DR. LEONARD G. PARSONS, Birmingham, England: I should like to ask Dr. Erb whether he has seen any case in which there was apparent cure. I observed a case in which the child apparently almost died with a secondary tumor of the skull. This child seemed to have recovered for a few weeks, but later succumbed.

DR. A. P. HART, Toronto: I encountered a case almost the same as Dr. Simpson's. In this child blindness developed along with symptoms which were not characteristic of a tumor of the brain. Finally a diagnosis of sarcoma was made. Permission to confirm this post mortem was not obtained.

DR. I. H. ERB, Toronto: Such a case as Dr. Parsons has described has never come under my observation.

A CASE OF SCLEREMA NEONATORUM. DR. J. F. MCINTOSH (by invitation), DR. T. R. WAUGH (by invitation) and DR. JESSIE BOYD SCRIVER, Montreal.

Sclerema neonatorum is relatively rare. It occurs in the first few weeks of life and is characterized by circumscribed or diffuse areas of solidified subcutaneous fat; softening and fluctuation of these areas have been observed, with occasional cyst formation.

A typical clinical case of this condition is presented together with histologic and biochemical studies of biopsy material obtained by excision and by aspiration.

Grossly, the skin was relatively normal, but in the subcutaneous tissue the fat had become transformed into a chalky white, rather lardaceous material. Histologically, characteristic doubly refractile acicular crystals were seen lying in tufts. They did not appear to take a scarlet red stain in frozen sections and were seen both inside and outside the fat lobules. In paraffin sections treated with eosin-hematoxylin stain, in response to this change in the fatty tissue there was seen marked widening of interlobular septums, due to fibroblastic proliferation and a certain amount of cellular exudate, and the formation of numerous foreign body giant cells, which wrap themselves about the crystals.

Chemical studies suggest that these crystals are probably neutral fat and not fatty acids. The iodine value confirms the relative saturation of the fatty acids present. Only a trace of cholesterol was demonstrated, and no lipase was present.

The blood findings were within the range of normal values for the young infant, and from them it appears that sclerema is not a general metabolic disease.

When the patient was 5 months old, calcification about one of the nodules was demonstrated by an x-ray picture; this was the only remaining lesion, the other scleremato us areas having disappeared.

DISCUSSION

DR. S. GRAHAM ROSS, Montreal: This case is very interesting because the distribution of the lesions was so diffuse. I have seen this type only in a newborn infant. It is recognized locally in the cheeks of new-born infants on forceps delivery. There has been considerable confusion in the terminology. I feel this condition should be differentiated from the generalized sclerema.

DR. D. P. ARNOLD, Buffalo: Has fat in the cheeks a different composition than that in the rest of the body?

DR. JESSIE BOYD SCRIVER, Montreal: I believe Dr. Arnold feels that his question has been answered, but these areas of sclerema were definitely circumscribed and quite different from others.

VITAMIN C REQUIREMENTS IN CHILDHOOD. DR. C. E. SNELLING, Toronto.

In a group of normal children observations have been made on the excretion of cevitamic acid in the urine under varying conditions. The cevitamic acid content of the blood has been investigated in a number of normal children and in children with scurvy. Six patients with scurvy have been observed who were treated with synthetic cevitamic acid.

The daily excretion of cevitamic acid in the urine varied widely with different children and in the same one on different days. No essential difference was observed related to the diet whether the child was on a normal diet or one low in vitamin C.

The utilization of synthetic and natural cevitamic acids shows no difference. The results do not indicate that the retention test is of value in all cases.

The reduced cevitamic acid content of the blood plasma did not indicate anything as to the vitamin C store of the subject.

Patients with scurvy improved much more rapidly with 2 ounces (59 cc.) of orange juice daily than with an equivalent amount of synthetic cevitamic acid.

DISCUSSION

DR. LEONARD G. PARSONS, Birmingham, England: There are one or two points I wish to mention. As to the therapeutic value of orange juice and cevitamic acid—the results which my co-workers and I obtain are exactly opposite. When from 500 to 1,000 mg. of cevitamic acid is given, the child is cured clinically in twenty-four hours. It should be stated that Harris does not say from 10 to 20 mg. is the dose for an infant. This is for a 10 stone (63.5 Kg.) man. I should like to ask also (1) regarding the measurement of reducing substances in the urine which interfere with the estimation of cevitamic acid and (2) whether there was any hemolysis in blood specimens.

I should, if I may be allowed, also like to enter a mild protest against the use of the term cevitamic acid. The American Medical Association does not like any cure to be suggested by name. The discoverer, Szent-Györgyi, named it hexuronic acid. Professor Harris has called this substance ascorbic acid.

DR. FREDERICK F. TISDALL, Toronto: In view of Dr. Parsons' very apt definement of the value of cevitamic acid and orange juice and the results reported by Dr. Snelling, it would be interesting to know the name of the firm manufacturing the form Dr. Parsons used and the one Dr. Snelling used.

DR. LEONARD G. PARSONS, Birmingham, England: Hoffmann-LaRoche, Inc.

DR. E. CHANT ROBERTSON, Toronto: I should like to ask whether Dr. Snelling has any evidence that the administration of salicylates affected the excretion of cevitamic acid. Is the synthetic vitamin C destroyed by boiling?

DR. C. E. SNELLING, Toronto: My associates and I have never given a child from 35 to 70 ounces (from 1 to 2 liters) of orange juice in one day. Using a dose equivalent to that we ordinarily employ for orange juice, we have not had the same effect with synthetic cevitamic acid. The reason I mention from 10 to 20 mg. is that Youmans named that amount, which is probably higher than that mentioned by Harris. With the interfering reducing factors in the urine we have had no experience. None of the blood specimens showed hemolysis. As to salicylates, I do not know whether they affect the excretion of cevitamic acid or not. The excretion is changed during rheumatic fever. If synthetic vitamin C stands or is shaken up, it becomes reduced. We have never boiled it.

AN UNUSUAL CASE OF CARBUNCLE OF THE BRAIN WITH RECOVERY. DR. H. M. KEITH, Montreal.

The patient was a girl of 5 years who contracted otitis media in December 1935, followed within a week by scarlet fever. The latter was complicated by mastoiditis on the left, and mastoidectomy was performed. After this facial paralysis developed on the left side, and the mastoid was explored again. After rather prolonged convalescence—approximately three months—she went home apparently well. Headache developed within twenty-four hours, and it was found that she had an increase of intracranial pressure. She had not the typical signs of cerebral abscess but showed widespread infection of the left temporal lobe at exploration. A portion of the left temporal lobe was removed, and the report includes a study of the specimen. The patient is perfectly well.

READ BY TITLE

MILIARY TUBERCULOSIS WITH APPARENT RECOVERY. DR. HENRY P. WRIGHT, Montreal.

Book Reviews

The Little Things in Life. By Barnett Sure, Ph.D. Price, $2.50. Pp. 340. New York: D. Appleton-Century Company, Inc., 1937.

This book contains, in popular and concentrated form, a survey of present day knowledge of vitamins, hormones and other minute essentials for health. After an introductory chapter on the deficiency diseases, the writer goes on with a discussion of "the vitamin alphabet," including interesting historical data and discussing the more important phases of present knowledge of vitamins. The two chapters on this subject, consisting of 91 pages, contain chiefly well established facts, presented in a style which should meet the approval both of the general reader and of the biologist. The latter might perhaps find statements with which he does not agree—for instance: "That mild scurvy is widespread in this country, not only in children but also among adults, is evidenced by unsound teeth, dental caries and diseased gums." On the whole, however, such controversial matter is treated separately in succeeding chapters which contain a discussion of vitamins and dental disorders, the relation of deficiencies in vitamins to colds and infections, etc. As these are subjects in which the laity is greatly interested, the discussion of them in a book of this kind is, of course, a necessity, although the presentation offers great difficulties.

A really critical review of the literature is, of course, out of the question in a book meant for the general reader, and the opposite, a wholesale acceptance of all published works, would be inadvisable, to say the least. The author steers a middle course, enumerating, mostly without discussion or comment, the results obtained by vitamin therapy in a great number of conditions. However, along frontiers of clinical research in vitamins the reports of positive, successful results always by far outnumber those of negative ones, although experience shows that few such successes are confirmed and permanently established. The mere reviewing of the literature without comment is, therefore, apt to give too optimistic a picture of the usefulness of vitamins, and one might perhaps have wished that the author had emphasized, for the benefit of the general reader, the controversial nature of some of the subjects under discussion. The man somewhat familiar with the field will, however, find much of interest in these chapters. In a chapter entitled "Vitamins in Infant Nutrition," the author gives detailed directions for the preparation of formulas, and in a following chapter the relation of malnutrition to deficiencies in vitamins is discussed. An 11 page table of vitamin contents of various foodstuffs concludes the part of the book dealing with vitamins (198 pages).

After some short chapters on minerals, allergy and intestinal ferments, the author proceeds with a discussion of the ductless glands. The chapter on this subject begins with an excellent popular presentation of the problem of diabetes and the history of the discovery of insulin (8 pages). This is followed by a discussion of hyperinsulinism or "hunger disease" (4 pages), with directions for the dietary treatment of the condition. The author also reviews favorable reports of the use of insulin in cases of pernicious vomiting in pregnancy, of poor appetite and of schizophrenia. Then follows a section on the thyroid gland, its function and disease; in discussing the treatment of the latter, the author shows commendable restraint and warns against the indiscriminate use of thyroid preparations. The remainder of the book deals with the parathyroids, the adrenals, the pituitary, etc., presenting mostly well established facts, in an interesting and critical manner.

To the physician who wants to refresh his memory on the subjects treated in this book "The Little Things in Life" can be highly recommended. In spite of the title, he will find not a trace of the gushing sensationalism which is typical of some popular publications. To the critical layman the book should prove interesting and easy reading.

Hearing and Speech in Deaf Children. Reports of the Hearing Committee of the Medical Research Council: V. Special Report Series, No. 221. By Phyllis M. T. Kerridge. Price, 2 shillings. Pp. 137. London: His Majesty's Stationery Office, 1937.

This report of a study of 456 moderately and severely deafened children from the schools for the deaf in London covers 137 pages and includes many charts and graphs. The purposes of the study were threefold: (1) to measure the deafness of deaf children by the more accurate, recently acquired methods; (2) to express the relation between deafness and speech in children, and (3) to estimate the benefit of magnified sounds to severely deaf children.

Of the 456 children, 128 were classed as partially deaf, since they could hear conversation at from 2 to 20 feet, while 328 were unable to hear conversation at 2 feet and were classed as deaf.

Of all the children studied, 42.5 per cent were born deaf, and the cause of deafness in the others was: otitis media associated with a specific fever in 18 per cent, of whom the majority had suffered from measles or scarlet fever; otitis media not associated with a specific fever in 16 per cent; meningitis in 6 per cent; congenital syphilis in 2.5 per cent and trauma in 1 per cent. The cause in 11.5 per cent was uncertain. Of those with severe deafness, there were 48 per cent born deaf, and of the rest 17 per cent were deaf from meningitis, 11.5 per cent from scarlet fever, 4 per cent each from measles, mumps and congenital syphilis and 2 per cent each from measles followed by whooping cough and scarlet fever followed by whooping cough. The cause in 7.5 per cent was unknown.

Only 3 per cent of the total number of children had no hearing to the audiometer test in either ear; 6 per cent had no hearing in one ear, and 10 per cent had no hearing for the "speech frequencies" (from 512 to 2048 double vibrations).

A comparison of air and bone conduction curves showed normal bone conduction in 100 per cent of cases of uniform loss of hearing for all tones due to otitis media, whereas in cases of high tone deafness bone conduction was normal in only 32 per cent of persons deaf because of otitis media and in only 3 per cent of those born deaf.

In studying the defects in speech it was found that minor defects occur among children who can hear conversation at several feet, but especially among those deaf for the high tones, where the sounds "s" and "sh" are omitted from words. In children who became deaf before the age of 2 years (before learning to talk), those with a loss of hearing not greater than 30 db. for the speech frequencies had normal speech; those with a hearing loss of from 30 to 50 db. had defects in speech in some cases. With greater losses in hearing the percentage of poor speech increased rapidly, between 90 and 100 per cent of the children with a loss of 90 db. having only poor or fair acquired speech.

The third part of the investigation was carried out by means of an electrical amplifier provided by the Multitone Electric Company. Each child operated his own volume control. The apparatus was used in teaching a group of 48 children for one year. At the end of that time, by comparing phonograph records of the child's speech before and after treatment, it was found that 44 per cent had benefited considerably; 19 per cent had benefited some; 16.5 per cent had only gained an appreciation of rhythm in speech with some educational benefit; 8 per cent had gained this appreciation of rhythm but without educational benefit, and 12.5 per cent had received no benefit.

Essentials of Electrocardiography for the Student and Practitioner of Medicine. By Richard Ashman, Ph.D., and Edgar Hull, M.D. Price, $3.50. Pp. 212, with 101 illustrations. New York: The Macmillan Company, 1937.

This book fulfils well the claims of its title, in that it offers a practical, concise exposition of the essential facts of electrocardiography. The first chapters, which describe the mechanics of taking an electrocardiogram and the theoretical meaning of the resulting curve, are clearly presented without the use of confusing technical terminology. One section of the book is devoted to a discussion of the normal

human electrocardiogram and is amplified by descriptions and illustrations of the commonest deviations from normal. The abnormalities commonly associated with rheumatic, syphilitic and arteriosclerotic types of cardiac disease are presented, and the value and the limitations of the electrocardiogram as a diagnostic factor in each of these diseases are discussed. The characteristic changes classically found in the conventional three leads of the electrocardiogram in coronary thrombosis, including the differentiation of anterior from posterior infarction, are well described and illustrated. The relative values of electrocardiographic findings in conditions such as hypertension, bacterial endocarditis and diphtheria are discussed briefly.

The authors recognize that chest leads are of definite value and devote a few pages to a discussion of their uses and interpretations. However, they deal with this subject somewhat inadequately, failing both to point out the present lack of standardization in the manner of taking chest leads and to explain that the differing types of curves obtained are due to variations in the placement of the electrodes on the chest and in the making of the connections on the limbs. Good illustrations showing the different types of chest leads in right and in left bundle branch block are shown, but chest leads in coronary thrombosis are not well described, and the illustrations are insufficient.

A final and proportionately large section of the book is devoted to an analysis of the disturbances of the cardiac mechanism. The arrhythmias are discussed fully and are clearly illustrated by characteristic electrocardiograms. The book is, in fact, generously illustrated throughout by well photographed and well selected curves.

The bibliography at the end of each chapter includes many of the more recent publications.

Although the authors have consistently followed their plan of keeping the presentation within the limits of practical application and have avoided involved technical discussions, the subject-matter is, in the most important respects, adequately covered.

Clinical Allergy Due to Foods, Inhalants, Contactants, Fungi, Bacteria and Other Causes: Manifestations, Diagnosis and Treatment. By Albert H. Rowe, M.D., Lecturer in Medicine in the University of California Medical School, San Francisco; Chief of the Clinic for Allergic Diseases of the Alameda County Health Center, Oakland, Calif.; President of the Association for the Study of Allergy, 1927-1928. Price, $8.50. Pp. 812, with 37 tables. Philadelphia: Lea & Febiger, 1937.

The ever widening field of allergy now touches practically every phase of clinical medicine. In the preface the author states: "Every physician, whether in general practice or in the specialties, is constantly confronted with allergic problems of varying severity and intensity according to his field of effort." Such problems make it imperative that physicians be acquainted with the subject of allergy, and with this in mind the author attempts to present the facts of clinical allergy in this volume in a convenient form for the practicing physician.

The general organization of the book, with a few exceptions, is good, but the construction of certain chapters is somewhat misleading. The most outstanding difference between this and most textbooks on the subject is that a chapter on treatment of food allergy by elimination diets and general measures follows the chapter on diagnosis and precedes those on the clinical entities of bronchial asthma, gastro-intestinal allergy, allergic dermatoses, etc. This places an overemphasis on foods in their relationship to other allergenic factors. In the chapter on bronchial asthma the entire subject of hay fever is discussed in detail, and two pages in a later chapter are devoted to nasal symptoms. The impression gathered is that pollen allergy is chiefly asthmatic. Certainly a clinical entity as important as hay fever deserves treatment in a more concrete manner.

The chapters on food and on gastro-intestinal allergy are excellent. The elimination diet and those in which wheat, milk or eggs have been avoided, together with the suggested menus, are extremely helpful. The author has drawn freely

from his large experience to give the reader several hundred workable diets which may be used in management of food allergies.

In the appendix are found the histories of 83 cases which are illustrative of some of the complications encountered in managing allergic patients. A voluminous and complete bibliography, including contributions up to 1937, completes this valuable book.

The book should be of value to general practitioner and specialist alike for its wealth of information presented in a style easily read and understood.

Anleitung zur Konstitutionsdiagnostik bei kindlicher Tuberkulose (an Hand von praktischen Beispielen). By Prof. Dr. Kurt Klare, Direktor der Tuberkulose-Kinderklinik Prinzregent-Luitpold Scheidegg-Allgau. Price, 4.35 marks. Pp. 56, with 22 illustrations. Leipzig: Georg Thieme, 1937.

Professor Klare points out the frequency with which various symptoms of nonspecific origin displayed by tuberculin-sensitive children of hyperreactive so-called exudative-lymphatic constitution lead to erroneous diagnoses of clinically active tuberculosis. He stresses the necessity of exercising judgment, based not only on information yielded by special laboratory and clinical studies but also on a comprehensive knowledge of inherent familial and individual traits, in correctly differentiating infected children who do from those who do not require institutional care. His vigorous remonstrance against the frequent failure of physicians to exercise discrimination in recommending the institutionalization of infected children unquestionably is sound.

In addition to the confusion in diagnosis occasioned by the exaggeration of clinical manifestations of specific and nonspecific infections characteristic of the exudative-lymphatic type of constitution, the tendency to hyperreaction has a prognostic significance, according to the author, in that the hypersensitivity exerts a favorable influence on the course of tuberculosis. Apparently, Professor Klare relies more on the character of the patient's constitution than on the type of tuberculosis that is present (primary or secondary) in making a prognosis. His failure to state the advisability of protecting all tuberculin-sensitive children from further infection probably is to be interpreted as evidence that he considers mention of this generally accepted prophylactic measure unnecessary.

The major portion of the monograph is devoted to the details of family and individual histories, laboratory and clinical findings and diagnosis in sixteen typical cases, which clearly illustrate the important points stressed in the introductory eleven pages. Nineteen reproductions of roentgenograms and three photographs accompany the text.

Erbgesundheitsgesetz und Ermittlung Kindlicher Schwachsinnszustände mit den Entwicklungstests von "Bühler-Hetzer." By Dr. E. Vowinckel. Unbound. Price, 3.40 marks. Pp. 54, with 28 illustrations. Stuttgart: Ferdinand Enke, 1936.

This monograph has a foreword by Prof. E. Rominger, of Kiel, Germany, in which he stresses the necessity of making a diagnosis of feeblemindedness early and with sufficient exactness to fit the statutes dealing with health heredity. The problem is most acute in the case of children who are not obviously feebleminded but who may be able to transmit feeblemindedness to their offspring.

Dr. Vowinckel discusses the limitations of the Binet-Simon intelligence tests and describes the advantages of the development tests proposed by Bühler and Hetzer, of Vienna. The approach in the latter is similar to that first suggested by Gesell, i. e., a comparison of the performance of the child in various activities with the criteria established for development at certain age levels. As dimensions of childhood activities, the following attributes were chosen: perception, body control, social attitude, learning power, deftness in doing things with the hand and mental creativeness.

From these tests, Bühler and Hetzer compared the developmental age with the chronological age to arrive at a developmental quotient. In addition to this quantitative estimation of development expressed numerically, they could also establish

a curve which would show the particular phases of development in which the child was good, superior or inferior. This curve is spoken of as the profile of development.

For persons who are interested in determining whether a child is backward in his general development, this monograph is helpful and presents a practicable method of procedure.

Quarterly Bulletin of the Health Organisation of the League of Nations. Price, $0.65. Pp. 176. New York: Columbia University Press, 1937.

The larger part of this book has to do with a new international insulin standard. Establishment of the new standard became necessary because the old standard was used up. The new standard has an activity of 22 units per milligram. This makes no significant change in the value of the unit.

Considerable space is given to the discussion of gas gangrene antitoxin. It is shown that gas gangrene antitoxin can be assayed with a high degree of accuracy. It is recommended that the permanent commission on biologic standardization accept the dry stable preparation of gas gangrene antitoxin of the Statens Serum Institute, Copenhagen, as the international standard for this antitoxin and define a unit in terms of this standard preparation for international use.

It is recommended that the stable preparation of diphtheria antitoxin, #788, prepared at the Statens Serum Institute, Copenhagen, be accepted as the international standard for use in the flocculation test. It is also proposed that work toward complete standardization of tetanus antitoxin be started. A method of preparing antipoliomyelitis convalescent serum for international use is discussed. In other chapters the labeling of preparations and the general methods of preparing standards are discussed, and there is a chapter on "A Simple Laboratory Method for the Desiccation of Serum and Other Protein Solutions."

Hemophilia. By Carroll LaFleur Birch. Price, paper, $2; cloth, $2.50. Pp. 150, with 23 plates and 74 charts. Urbana, Ill.: University of Illinois Press, 1937.

In this monograph the history, the diagnosis and the course of hemophilia and the condition of the blood are discussed briefly but completely, and there are excellent illustrative plates. The major part of the book consists of the histories of ninety-eight patients, with seventy-five genealogical charts. These charts have been painstakingly compiled, and the family histories have been followed back an amazing distance. One, for example, carries the family back to 1638. So far as possible, controversial matter has been avoided, and the discussion is limited to verified data.

The book represents the fruit of nine years' study by the author, and never before has such a mass of statistics been obtained on hemophilia. Dr. Birch can well be proud of this work. Incidentally, the printing, the illustrations and the binding of the book have been beautifully done.

Registro e Interpretacion de la Actividad Cardiovascular del Lactante Normal. By Angel S. Segura. Paper. Pp. 118, with 41 tables and 23 illustrations. Cordoba, Argentina: the University of Cordoba, 1937.

This book contains the records of the phonocardiographic heart sounds of infants and young children, optical tracings of the fontanellar pulse and of the femoral and the tibial pulse and records of the cardiac rate and rhythm. It is an exceptionally fine piece of work and although written in Spanish can easily be understood by any one interested in the subject.

Rapport sur le service des enfants assistés du Département de la Seine, 1935. Part II. By Dr. Louis Mourier. Pp. 69, with 14 tables (no. 18 to 31). Paris: Administration générale de l'assistance publique à Paris, 1936.

This is the financial report of the Director of the Administration of Public Assistance for the Department of the Seine for 1935. The report of the work done in 1935 in the supervision of health and in the aid and supervision given to dependents has already appeared and has been reviewed for this journal.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Herreplein, Groningen, Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. L. Emmett Holt Jr., Johns Hopkins Hospital, Baltimore.
Canadian Committee:
Chairman: Dr. H. B. Cushing, 1390 Sherbrooke St., W., Montreal.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.
Place: Rome, Italy. Time: Oct. 4-8, 1937.

FOREIGN

British Paediatric Association

President: Dr. J. Wilkie Scott, 40 The Rope Walk, Nottingham, England.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Clifford D. Sweet, 2940 Summit St., Oakland, Calif.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: San Francisco. Time: June 13-17, 1938.

American Academy of Pediatrics

President: Dr. Philip Van Ingen, 125 E. 71st St., New York.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Boston, Mass. Time: Nov. 12-13, 1937.
Region II. Place: New Orleans, La. Time: Nov. 30-Dec. 1-3, 1937.
Region III. Place: Lake Shore Athletic Club, Chicago. Time: Oct. 14-16, 1937.
Region IV. Place: Los Angeles, Calif. Time: Nov. 4-6, 1937.

American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

American Pediatric Society

President: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: The Sagamore, Bolton Landing, New York. Time: June 9-11, 1938.

Canadian Society for the Study of Diseases of Children

President: Dr. Alton Goldbloom, 1543 Crescent St., Montreal, Quebec.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

Society for Pediatric Research

President: Dr. Samuel Z. Levine, 525 E. 68th St., New York.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.
Place: Seattle. Time: Last Saturday in January 1938.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Gilbert Levy, 20 S. Dunlap St., Memphis, Tenn.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Place: New Orleans. Time: Nov. 30-Dec. 3, 1937.

STATE

Alabama Pediatric Society

President: Dr. J. H. Baumhauer, 56 St. Joseph St., Mobile.
Secretary-Treasurer: Dr. M. Vaun Adams, 803 Government St., Mobile.
Place: Mobile. Time: Third Monday in April 1938.

Arkansas State Pediatric Association

Chairman: Dr. E. C. McMullen, 500 Main St., Pine Bluff.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Texarkana, Ark. Time: February 1938.

California State Medical Society, Section on Pediatrics

Chairman: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Secretary: Dr. Hartzel H. Ray, 23-2nd Ave., San Mateo.
Place: Pasadena. Time: May 9-12, 1938.

Florida State Pediatric Society

President: Dr. Douglas D. Martin, 442 W. Lafayette St., Tampa.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Place: Augusta. Time: April 1938.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. J. Harold Root, 103 N. Main St., Waterbury.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Indiana State Pediatric Society

President: Dr. Ernest R. Carlo, 2902 Fairfield Ave., Fort Wayne.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

Louisiana State Pediatric Society

President: Dr. Clarence H. Webb, 624 Travis St., Shreveport.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Place: New Orleans. Time: April 25-27, 1938.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. John D. Craig, 33 E. 61st St., New York.
Secretary: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Place: New York. Time: May 9-12, 1938.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Secretary: Dr. Ward Chadwick, 524 Medical Arts Bldg., Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Cawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. John LaBruce Ward, Arcade Bldg., Asheville.
Secretary: Dr. Lewis Elias, 36 Grove St., Asheville.

Oklahoma State Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

Pennsylvania Medical Society, Pediatric Section

Chairman: Dr. Theodore O. Elterich, 3700 Fifth Ave., Pittsburgh.
Secretary: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Place: Philadelphia. Time: Oct. 5-7, 1937.

South Carolina Pediatric Society

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

Tennessee State Pediatric Society

President: Dr. Eugene Rosamond, 1074 Madison Ave., Memphis.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Nashville. Time: April 12-14, 1938.

Texas Pediatric Society

President: Dr. John G. Young, 3930 McKinney Ave., Dallas.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Galveston. Time: May 10-12, 1938.

Virginia Pediatric Society

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, Weston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Secretary: Dr. Arthur J. Horesh, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Secretary: Dr. Samuel T. Levethan, 254 E. 184th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Walter D. Ludlum, 1421 Cortelyou Rd., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave., Chicago. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. John Young, 3930 McKinney Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. W. J. Scott, 5140–2nd Ave., Detroit.
Secretary: Dr. Harold E. Clark, 100 Atkinson Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. T. F. Davenport, 104 Ponce de Leon Ave., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Penny Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385—24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 1020 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry R. Litchfield, 163 Eastern Parkway, Brooklyn.
Secretary: Dr. Jacob Rosenblum, 550 Ocean Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144—38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. David W. Goltman, 1073 Madison Ave., Memphis, Tenn
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. George F. Kelly, 425 E. Wisconsin St., Milwaukee.
Secretary: Dr. Helen Jane Zilmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Henry E. Utter, 122 Waterman St., Providence, R. I.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meeting a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Samuel Z. Levine, 525 E. 68th St., New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Alternate months.

Philadelphia Pediatric Society

President: Dr. Emily Bacon, 2104 Spruce St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200—5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Lee E. Sutton Jr., 2601 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. James E. Russell Jr., 820 Metropolitan Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Frank H. Douglass, Medical Dental Bldg., Seattle.
Secretary: Dr. C. Luverne Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Louis M. Earle, 6381 Hollywood Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. M. Cooperstock, Northern Michigan Children's Clinic, Marquette.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor. Time: Nov. 19-20, 1937.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. R. A. Higgons, 264 King St., Port Chester, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, October, December, February and April.